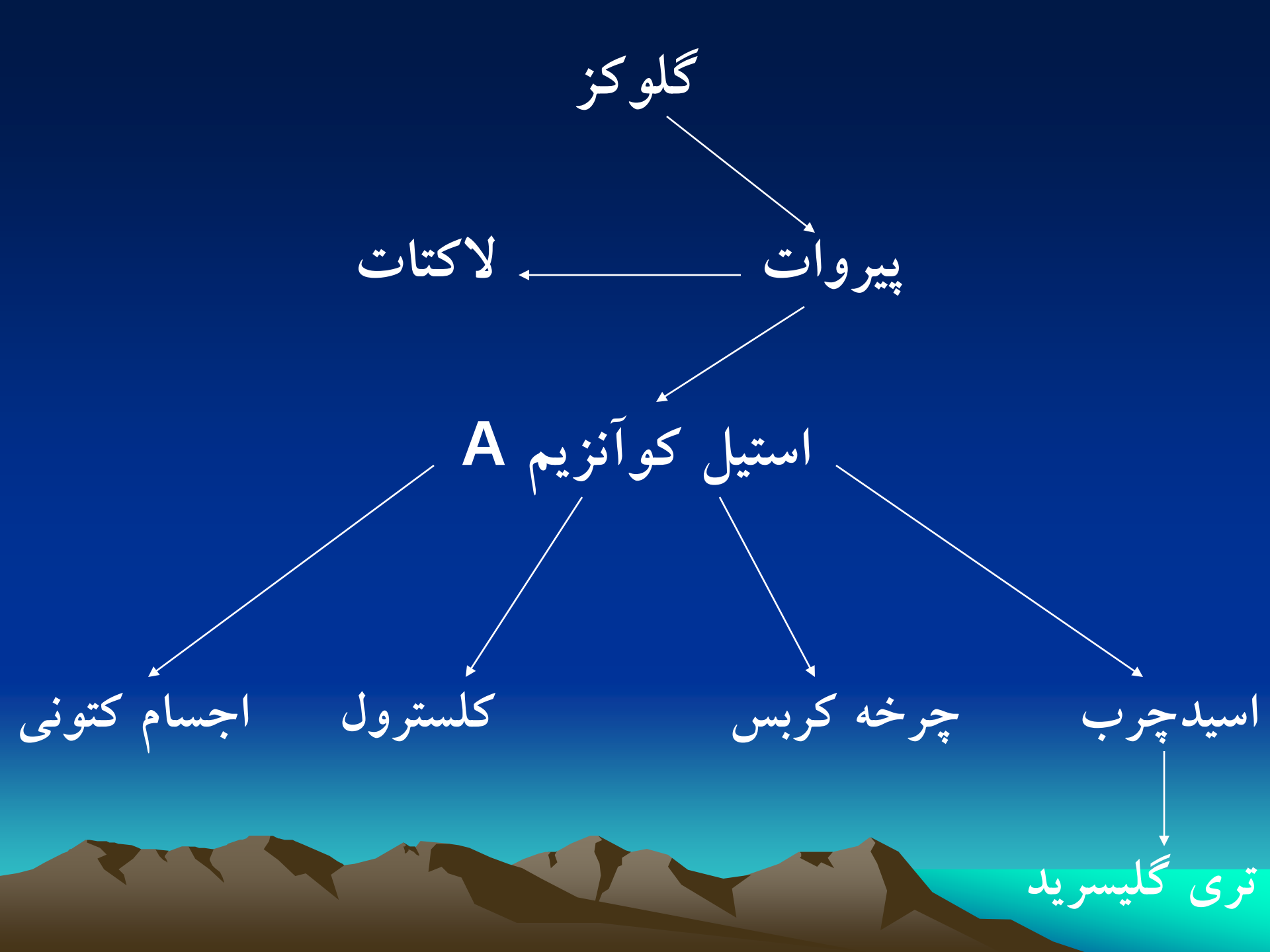
Carbohydrat Metabolism

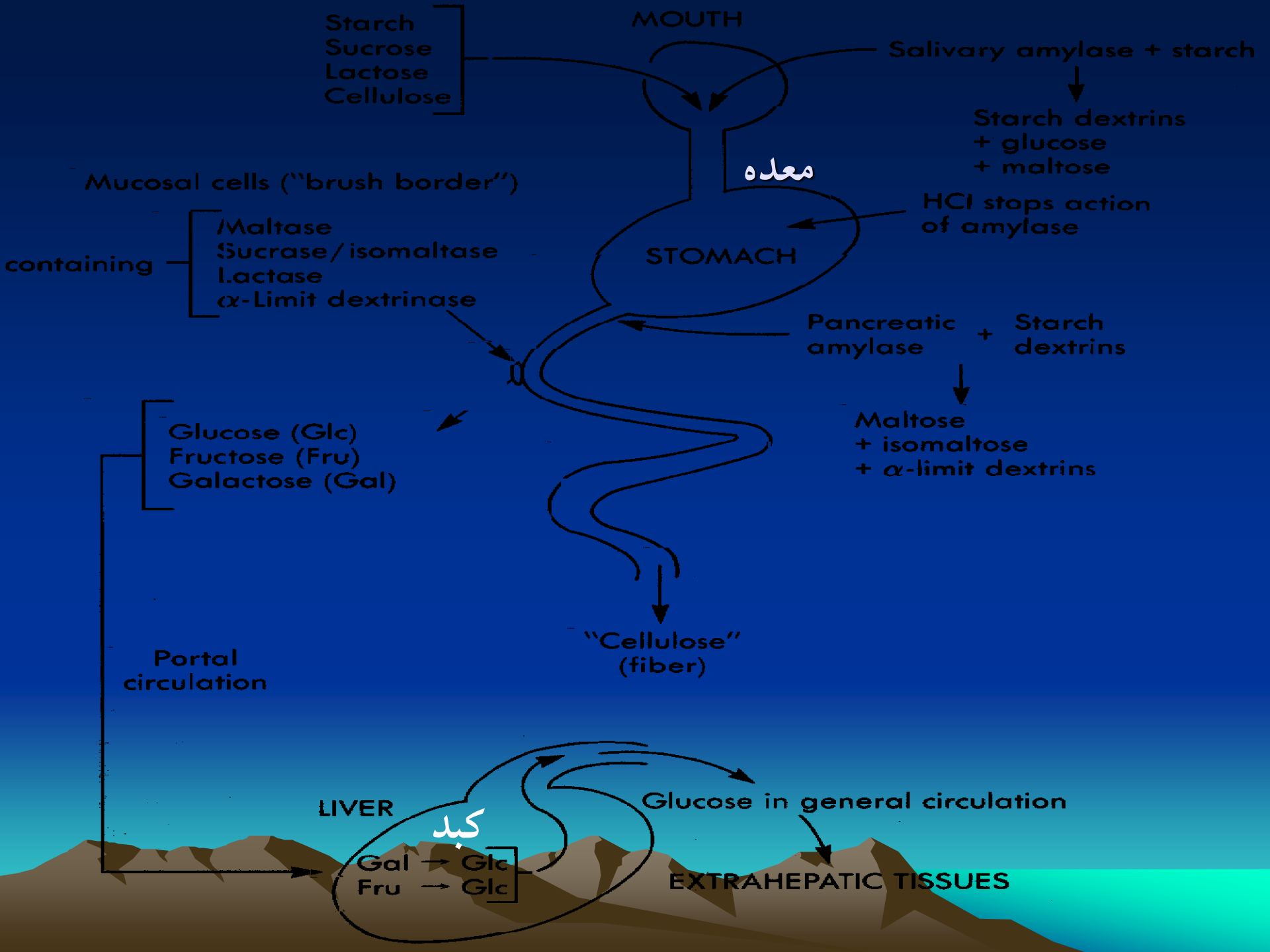

گلوکز
پیروات
لاکتات
استیل کوآنزیم A
اجسام کتونی
کلسترول
چرخه کربس
اسیدچرب
تری گلیسرید

- گلیکولیز
- گلیکوژنز
- گلیکوژنولیز
- مسیر پنتوز فسفات
- گلوکونئوژنز
- لیپوژنز
- لیپولیز

Digestion & Carbohydrate Absorbtion

Table 19–2. Glucose transporters.

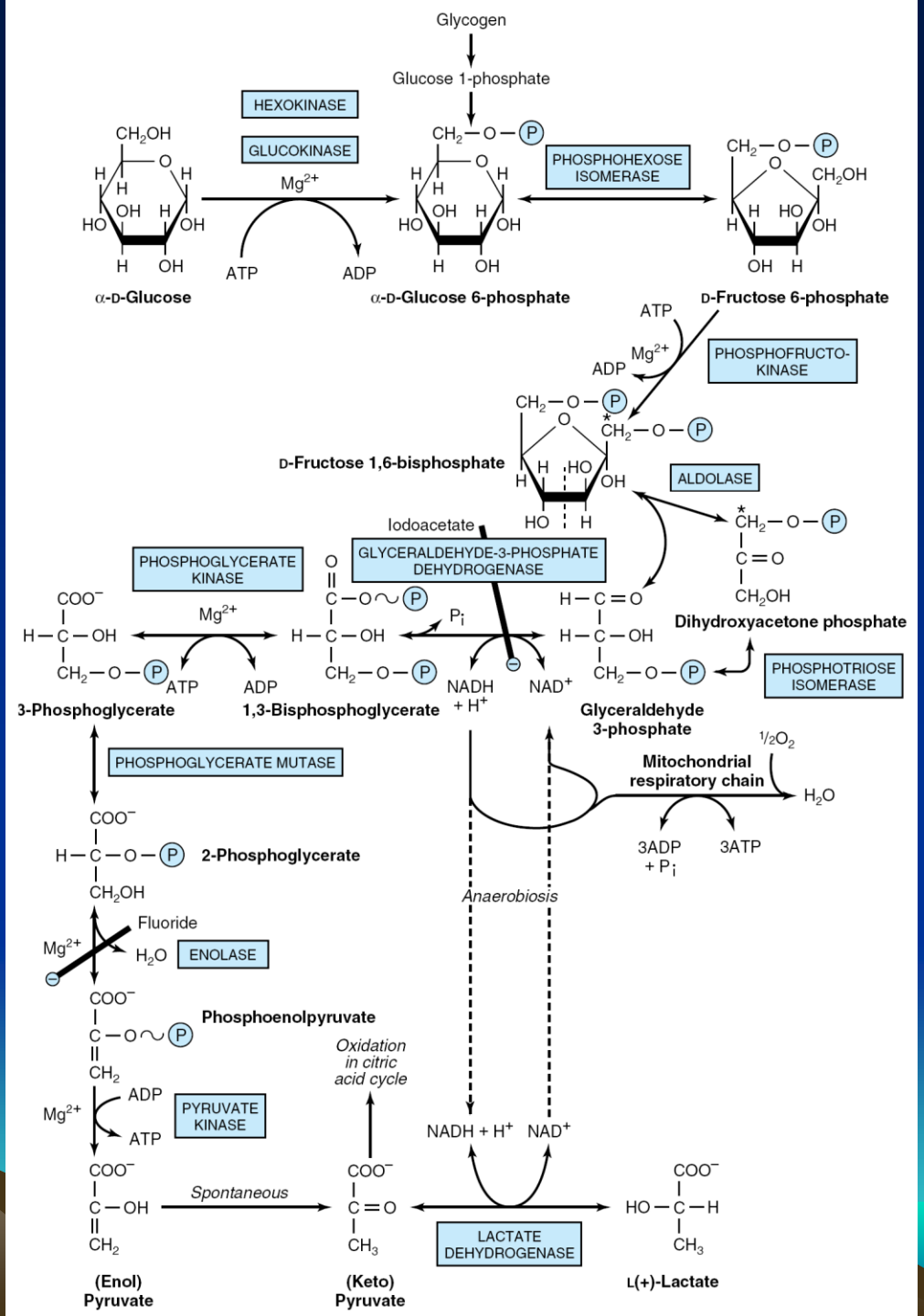
	Tissue Location	Functions
Facilitative bidirectional transporters		
GLUT 1	Brain, kidney, colon, placenta, erythrocyte	Uptake of glucose
GLUT 2	Liver, pancreatic B cell, small intestine, kidney	Rapid uptake and release of glucose
GLUT 3	Brain, kidney, placenta	Uptake of glucose
GLUT 4	Heart and skeletal muscle, adipose tissue	Insulin-stimulated uptake of glucose
GLUT 5	Small intestine	Absorption of glucose
Sodium-dependent unidirectional transporter		
SGLT 1	Small intestine and kidney	Active uptake of glucose from lumen of intestine and reabsorption of glucose in proximal tubule of kidney against a concentration gradient


Starch
Sucrose
Lactose
Cellulose
MOUTH
Salivary amylase + starch
Starch dextrins
+ glucose
+ maltose
معده
Mucosal cells ("brush border")
containing
Maltase
Sucrase/isomaltase
Lactase
α-Limit dextrinase
HCl stops action
of amylase
STOMACH
Pancreatic
amylase
+
Starch
dextrins
Maltose
+ isomaltose
+ α-limit dextrins
Glucose (Glc)
Fructose (Fru)
Galactose (Gal)
"Cellulose"
(fiber)
Portal
circulation
LIVER
کبد
Gal → Glc
Fru → Glc
Glucose in general circulation
EXTRAHEPATIC TISSUES

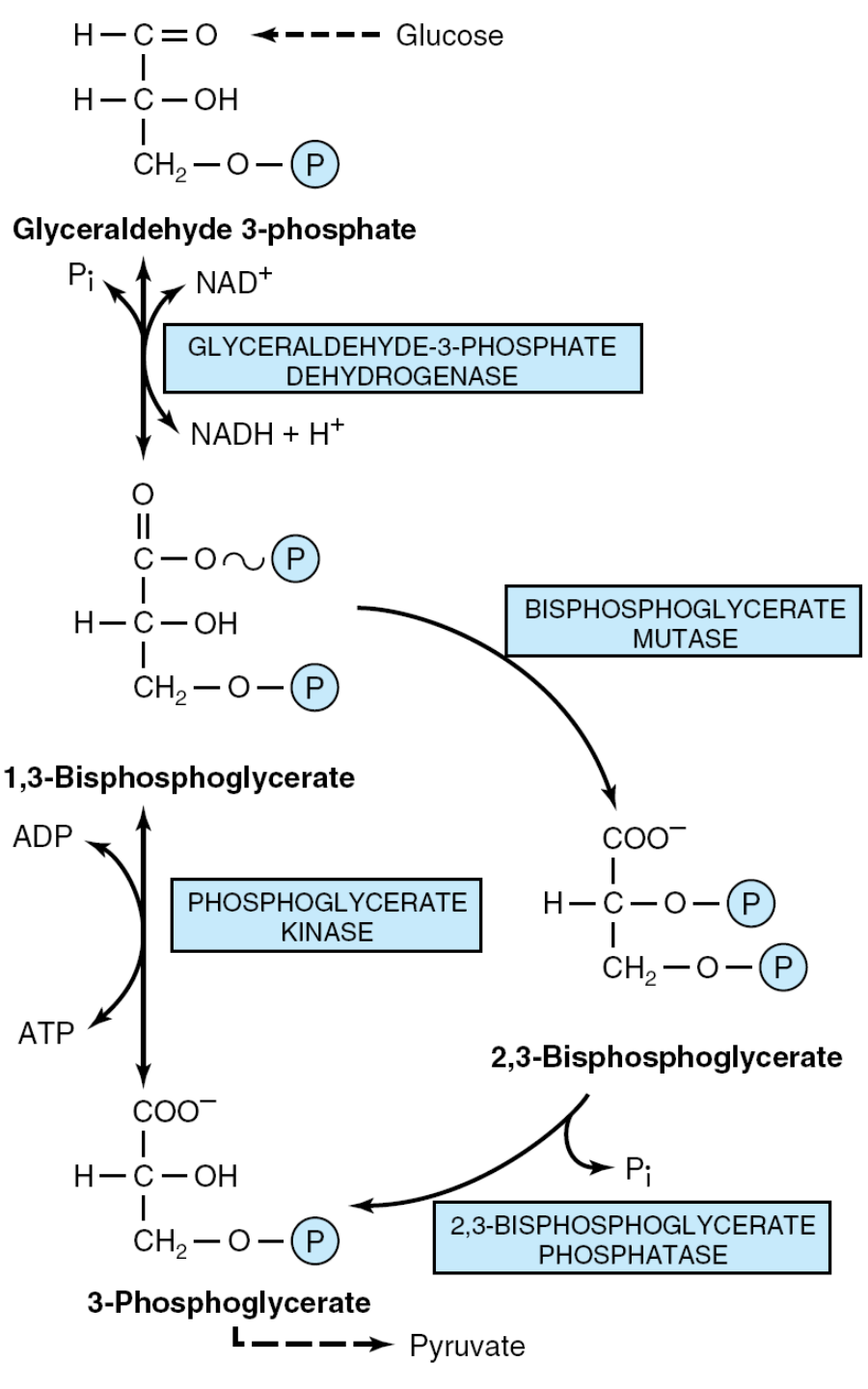
گلیکولیز

گلوکز + 2ADP + $2P_i$ + $2NAD^+$

دو مولکول پیروات + 2ATP + 2NADH + $2H^+$


Glycogen
Glucose 1-phosphate
HEXOKINASE
GLUCOKINASE
Mg2+
ATP
ADP
α-D-Glucose
α-D-Glucose 6-phosphate
PHOSPHOHEXOSE ISOMERASE
D-Fructose 6-phosphate
ATP
Mg2+
ADP
PHOSPHOFRUCTO-KINASE
D-Fructose 1,6-bisphosphate
ALDOLASE
Iodoacetate
GLYCERALDEHYDE-3-PHOSPHATE DEHYDROGENASE
PHOSPHOGLYCERATE KINASE
Dihydroxyacetone phosphate
Pi
NADH + H+
NAD+
3-Phosphoglycerate
1,3-Bisphosphoglycerate
Glyceraldehyde 3-phosphate
PHOSPHOTRIOSE ISOMERASE
PHOSPHOGLYCERATE MUTASE
1/2O2
Mitochondrial respiratory chain
H2O
3ADP + Pi
3ATP
2-Phosphoglycerate
Anaerobiosis
Fluoride
H2O
ENOLASE
Phosphoenolpyruvate
Oxidation in citric acid cycle
ADP
ATP
PYRUVATE KINASE
NADH + H+
NAD+
Spontaneous
LACTATE DEHYDROGENASE
(Enol) Pyruvate
(Keto) Pyruvate
L(+)-Lactate

Rapaport Shunt

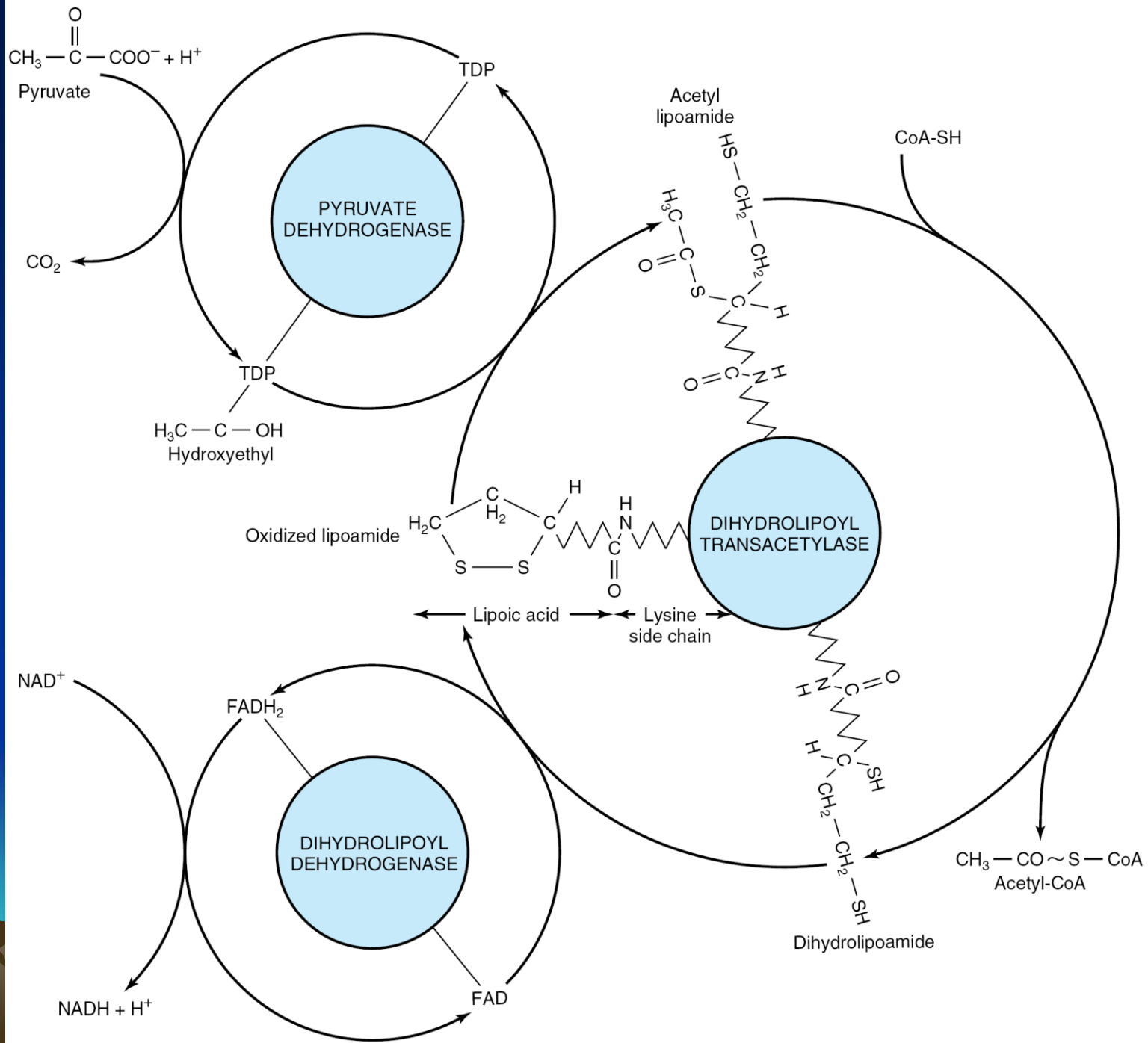


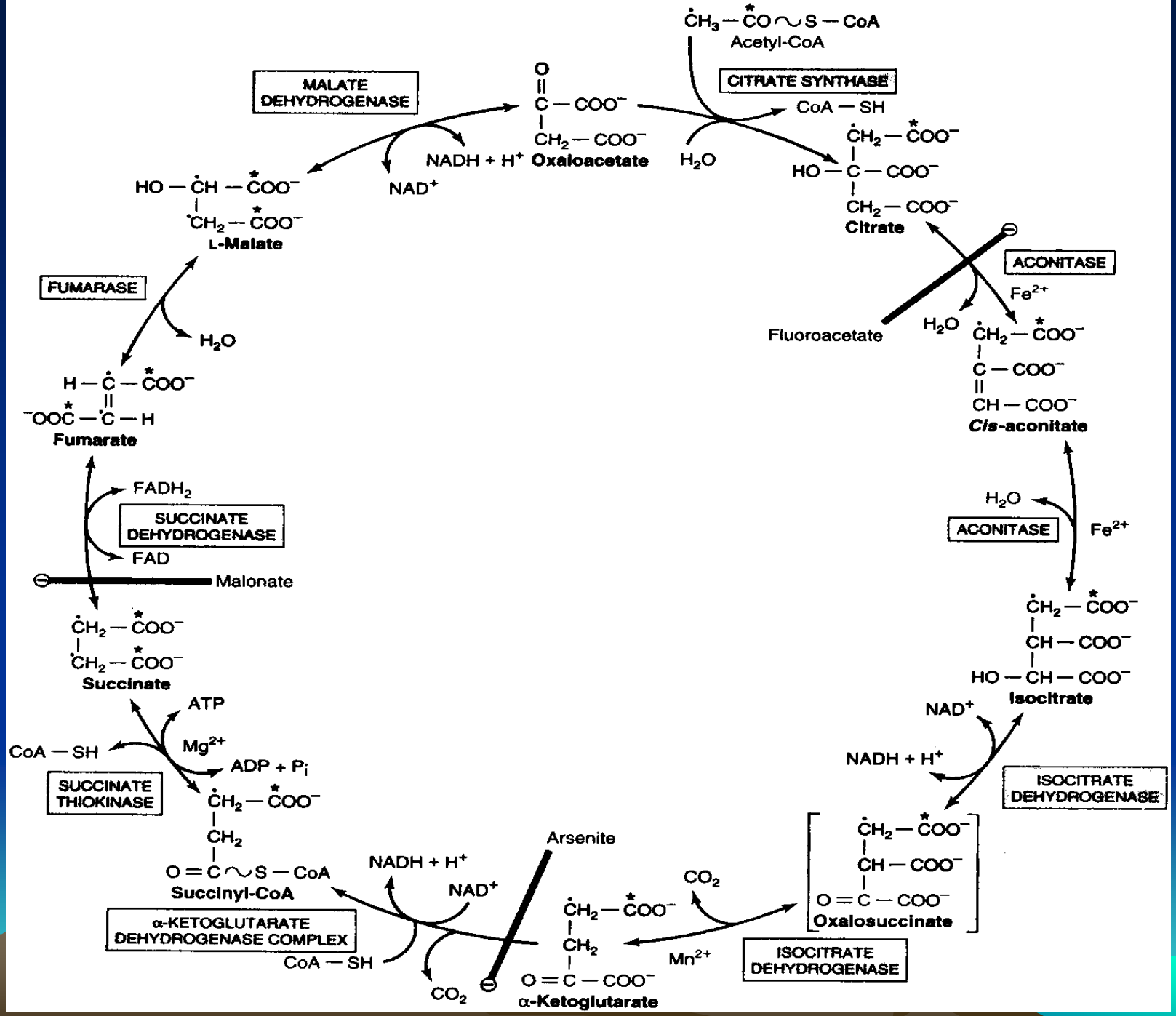
تبدیل پیروات به استیل کوآنزیم A

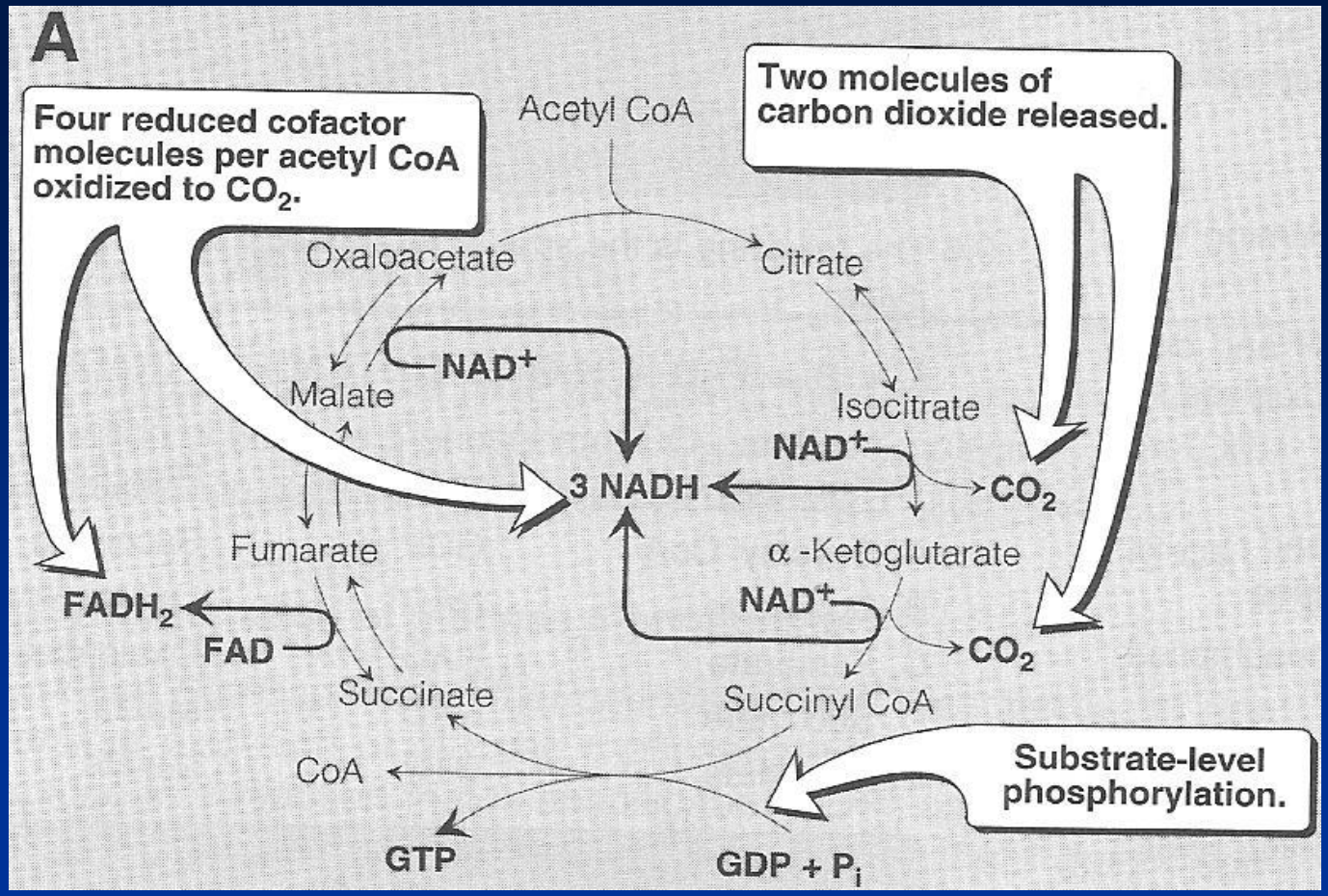
پیروات + کوآنزیمA + $2NAD^+$

↓

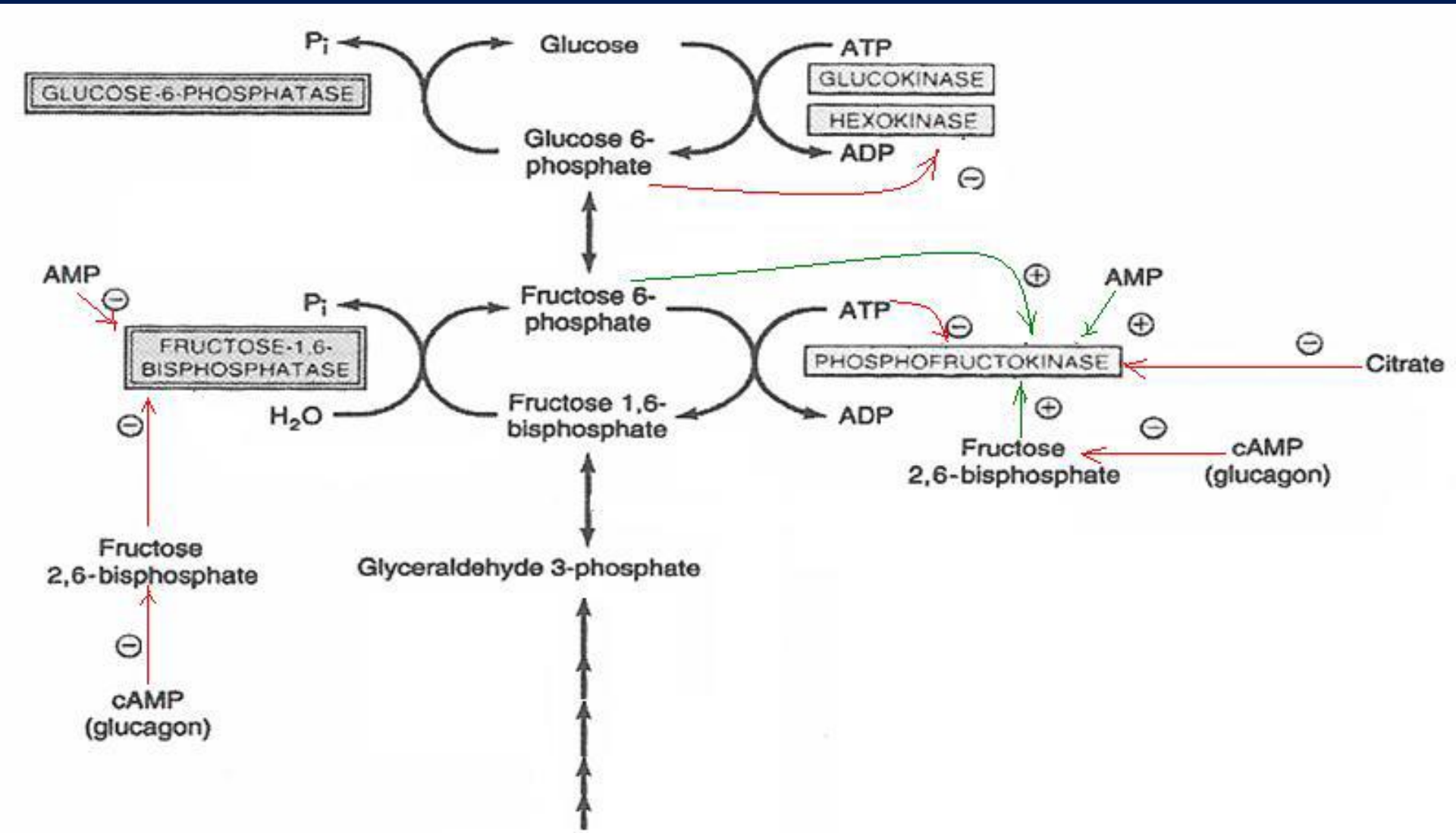
استیل کوآنزیمA + $2CO_2$ + $2NADH$ + $2H^+$

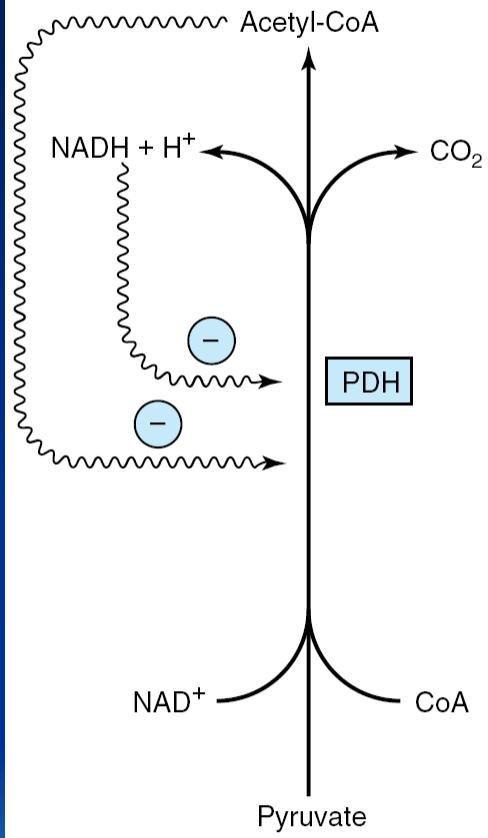

Pyruvate
TDP
PYRUVATE DEHYDROGENASE
CO_2
TDP
Hydroxyethyl
Acetyl lipoamide
CoA-SH
Oxidized lipoamide
DIHYDROLIPOYL TRANSACETYLASE
Lipoic acid
Lysine side chain
NAD^+
$FADH_2$
DIHYDROLIPOYL DEHYDROGENASE
$NADH + H^+$
FAD
Acetyl-CoA
Dihydrolipoamide


Acetyl-CoA
CITRATE SYNTHASE
CoA — SH
Oxaloacetate
H2O
MALATE DEHYDROGENASE
NADH + H+
NAD+
L-Malate
Citrate
ACONITASE
Fe2+
H2O
Fluoroacetate
Cis-aconitate
FUMARASE
H2O
Fumarate
FADH2
SUCCINATE DEHYDROGENASE
FAD
Malonate
ACONITASE
Fe2+
H2O
Succinate
Isocitrate
ATP
Mg2+
ADP + Pi
CoA — SH
SUCCINATE THIOKINASE
NAD+
NADH + H+
ISOCITRATE DEHYDROGENASE
Succinyl-CoA
Arsenite
NADH + H+
NAD+
CO2
α-KETOGLUTARATE DEHYDROGENASE COMPLEX
CoA — SH
CO2
Mn2+
ISOCITRATE DEHYDROGENASE
α-Ketoglutarate
Oxalosuccinate

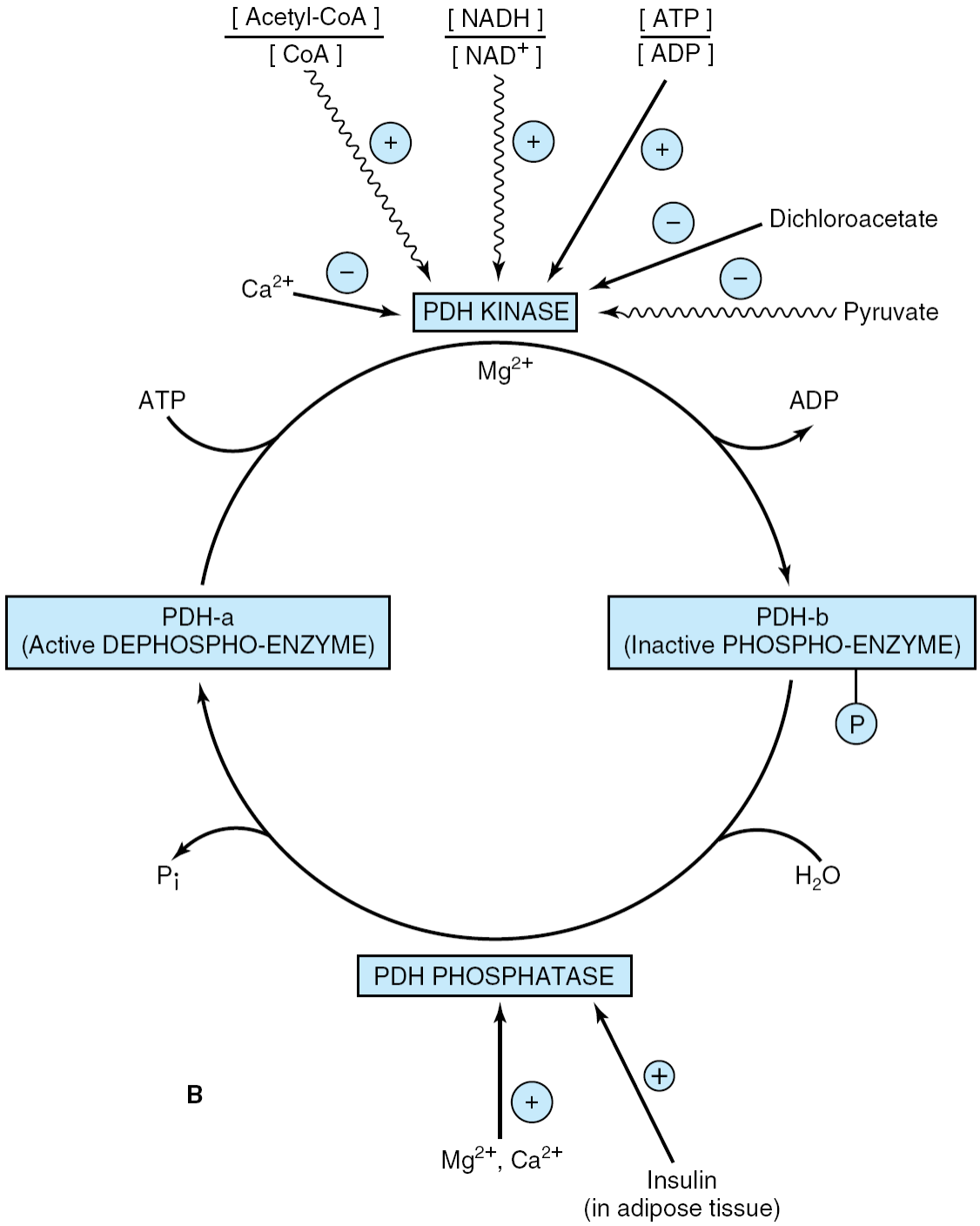


Energy-producing reaction	Number of ATP produced
3 NADH ⟶ 3 NAD^+	9
$FADH_2$ ⟶ FAD	2
GDP + P_i ⟶ GTP	1
	12 ATP/acetyl CoA oxidized

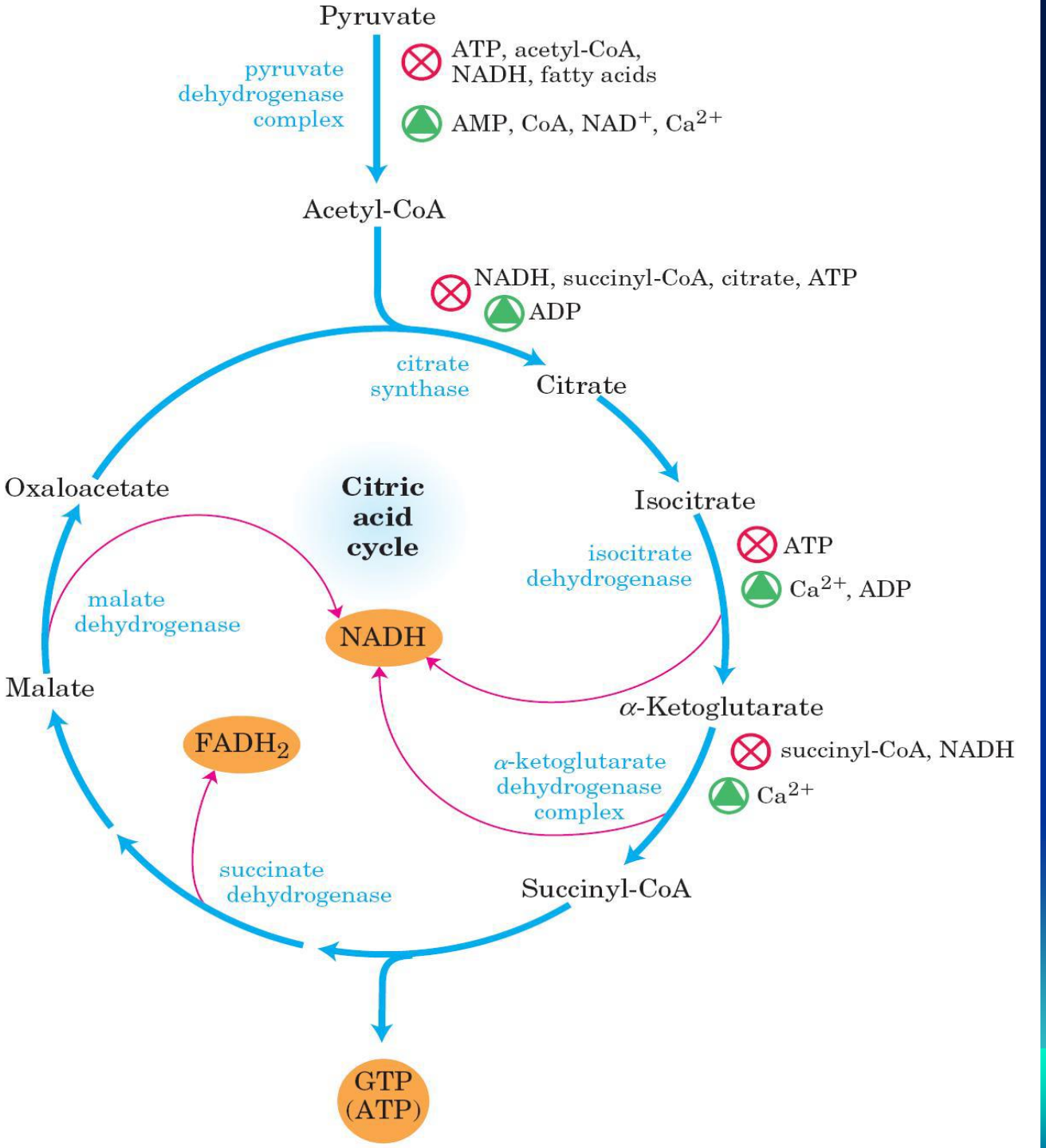

Pi
Glucose
ATP
GLUCOSE-6-PHOSPHATASE
GLUCOKINASE
HEXOKINASE
Glucose 6-phosphate
ADP
AMP
Pi
Fructose 6-phosphate
ATP
AMP
FRUCTOSE-1,6-BISPHOSPHATASE
PHOSPHOFRUCTOKINASE
Citrate
H2O
Fructose 1,6-bisphosphate
ADP
Fructose 2,6-bisphosphate
cAMP (glucagon)
Fructose 2,6-bisphosphate
Glyceraldehyde 3-phosphate
cAMP (glucagon)


Acetyl-CoA
NADH + H+
CO2
PDH
NAD+
CoA
Pyruvate

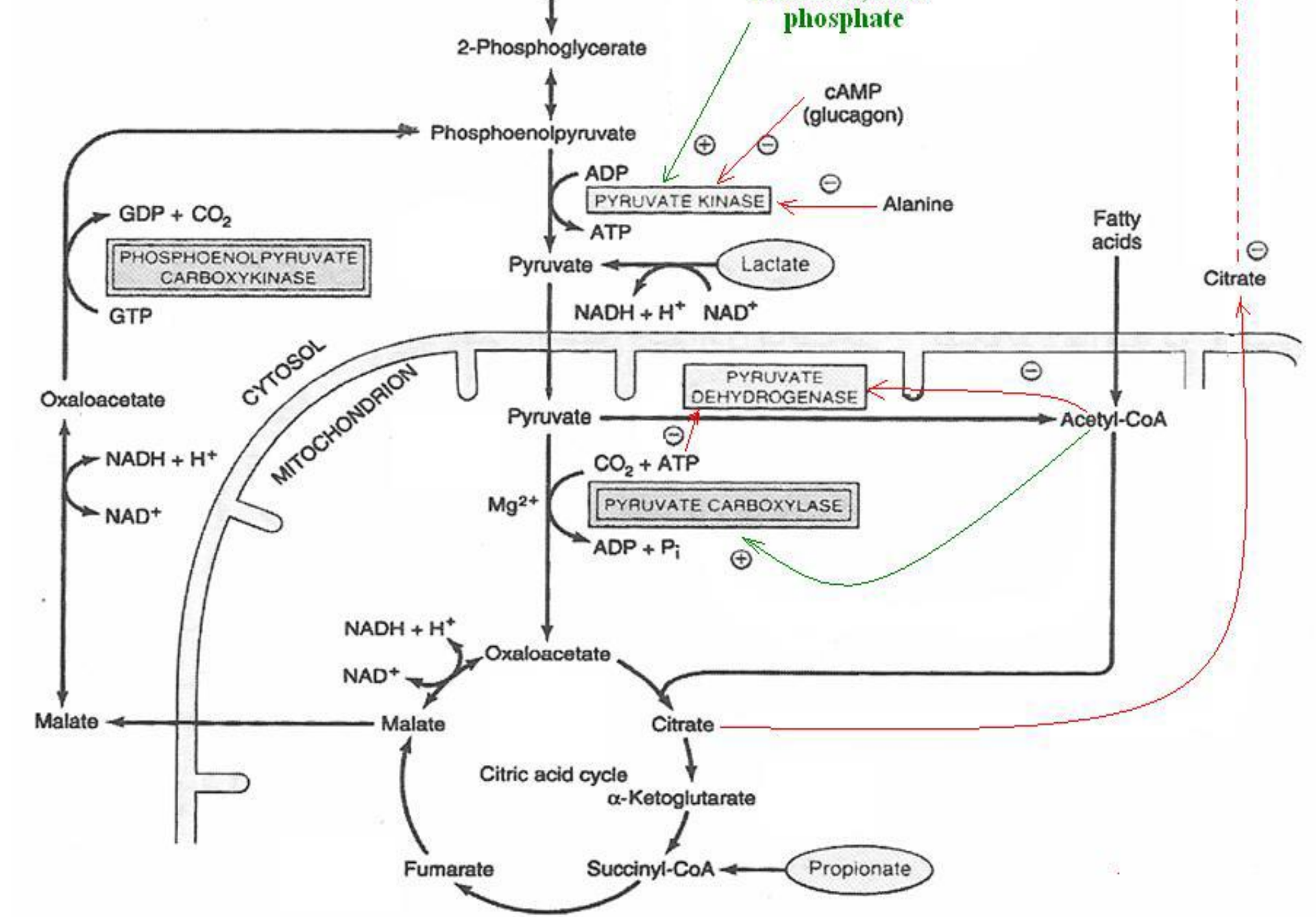
A

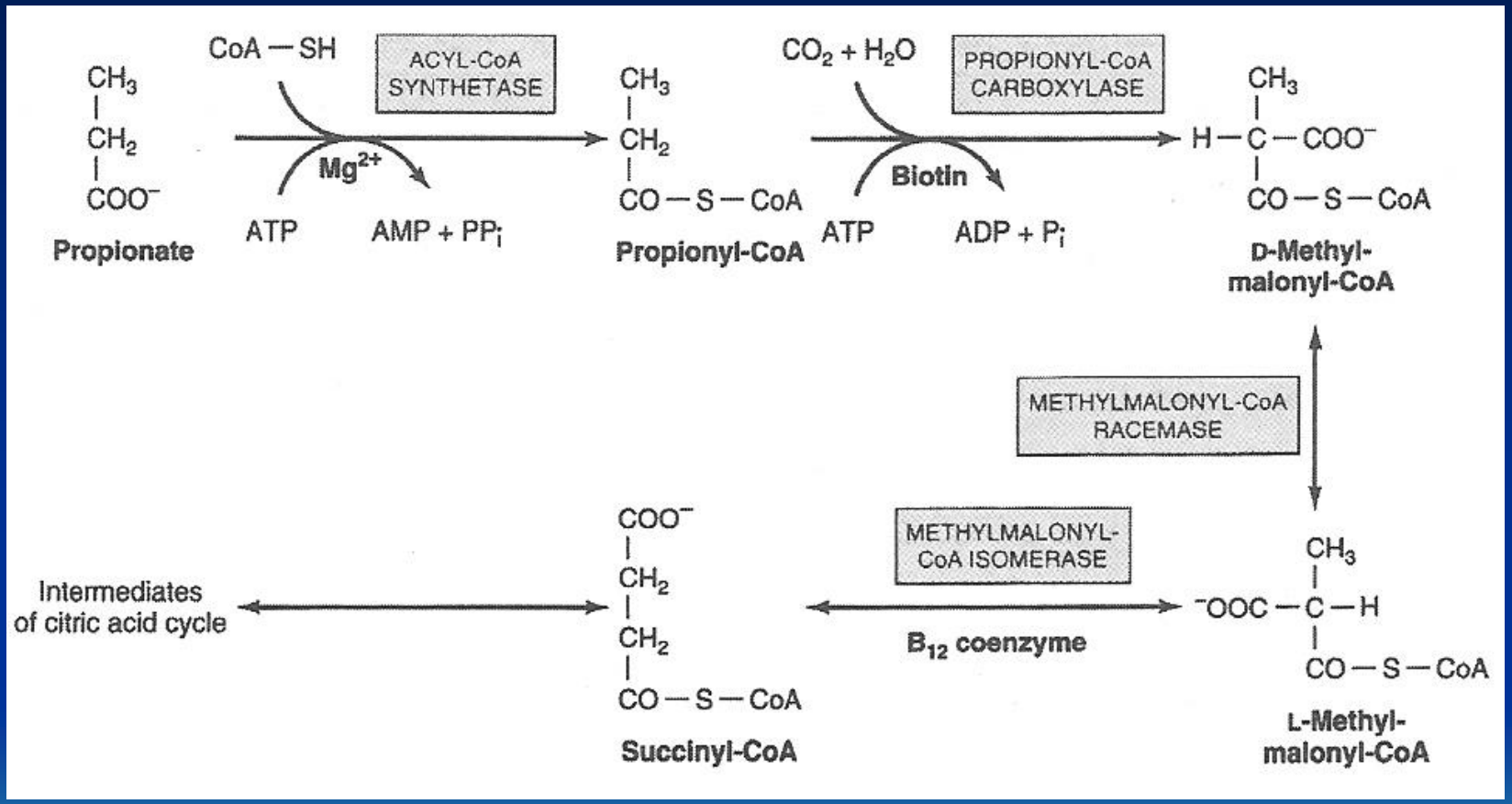

[Acetyl-CoA] / [CoA]
[NADH] / [NAD+]
[ATP] / [ADP]
Dichloroacetate
Ca2+
PDH KINASE
Pyruvate
Mg2+
ATP
ADP
PDH-a
(Active DEPHOSPHO-ENZYME)
PDH-b
(Inactive PHOSPHO-ENZYME)
P
Pi
H2O
PDH PHOSPHATASE
Mg2+, Ca2+
Insulin
(in adipose tissue)

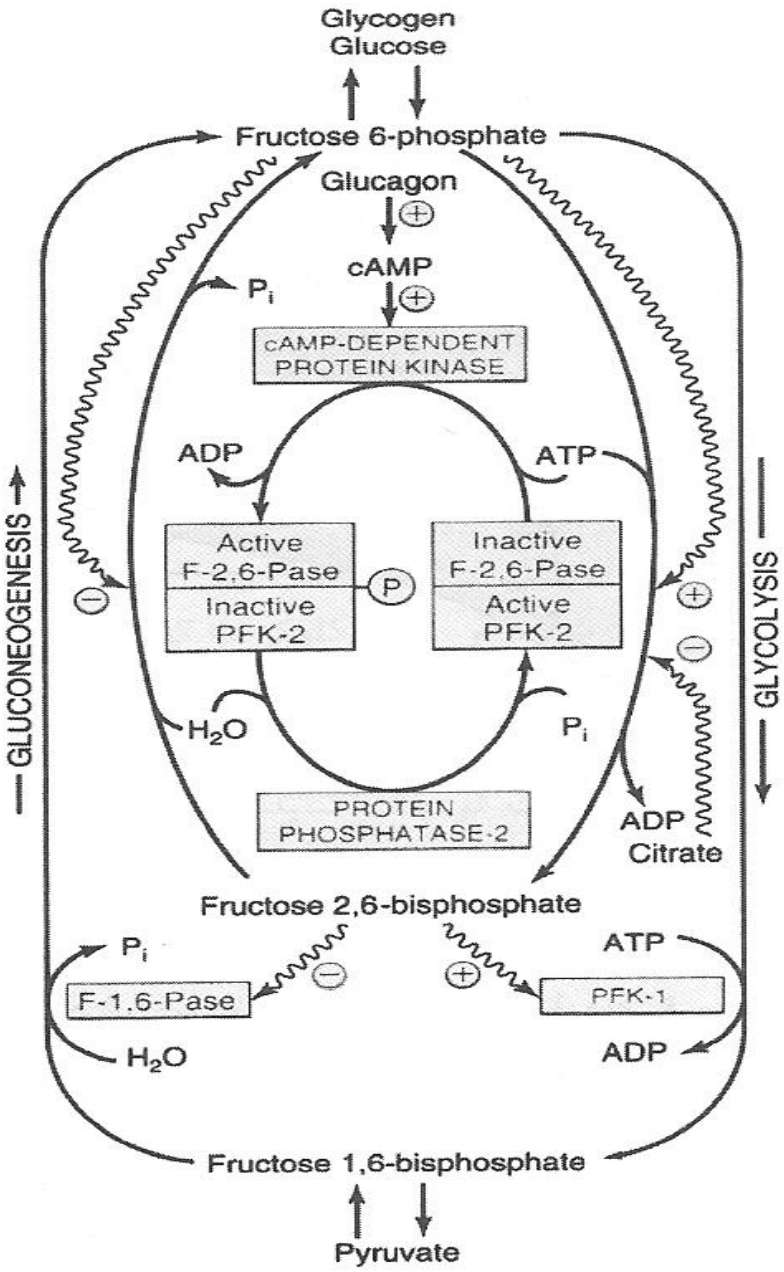
B


Pyruvate
pyruvate dehydrogenase complex
ATP, acetyl-CoA, NADH, fatty acids
AMP, CoA, NAD+, Ca2+
Acetyl-CoA
NADH, succinyl-CoA, citrate, ATP
ADP
citrate synthase
Citrate
Isocitrate
ATP
Ca2+, ADP
isocitrate dehydrogenase
α-Ketoglutarate
succinyl-CoA, NADH
Ca2+
α-ketoglutarate dehydrogenase complex
Succinyl-CoA
GTP (ATP)
succinate dehydrogenase
FADH2
Malate
malate dehydrogenase
NADH
Oxaloacetate
Citric acid cycle

Gluconeogenesis


phosphate
2-Phosphoglycerate
cAMP
(glucagon)
Phosphoenolpyruvate
ADP
PYRUVATE KINASE
Alanine
ATP
GDP + CO2
PHOSPHOENOLPYRUVATE CARBOXYKINASE
GTP
Pyruvate
Lactate
NADH + H+
NAD+
Fatty acids
Citrate
CYTOSOL
MITOCHONDRION
PYRUVATE DEHYDROGENASE
Oxaloacetate
Pyruvate
Acetyl-CoA
NADH + H+
NAD+
CO2 + ATP
Mg2+
PYRUVATE CARBOXYLASE
ADP + Pi
NADH + H+
NAD+
Oxaloacetate
Malate
Malate
Citrate
Citric acid cycle
α-Ketoglutarate
Fumarate
Succinyl-CoA
Propionate


CoA — SH
ACYL-CoA SYNTHETASE
Mg2+
ATP
AMP + PPi
Propionate
Propionyl-CoA
CO2 + H2O
PROPIONYL-CoA CARBOXYLASE
Biotin
ATP
ADP + Pi
D-Methyl-malonyl-CoA
METHYLMALONYL-CoA RACEMASE
METHYLMALONYL-CoA ISOMERASE
B12 coenzyme
Intermediates of citric acid cycle
Succinyl-CoA
L-Methyl-malonyl-CoA



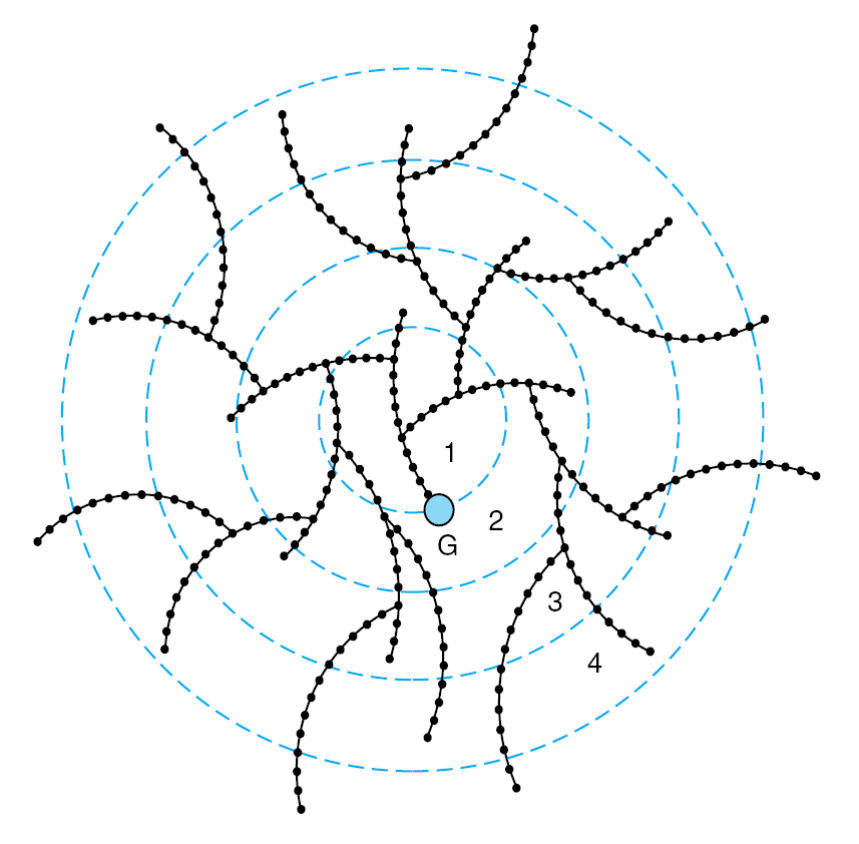
شکل ۳-۱۹. کنترل گلیکولیز و گلوکونئوژنز در کبد توسط فروکتو
۶،۲-بیس‌فسفات و آنزیم دوکاره PFK/F-2,6-Pase (۶-فسفوفروکتو-۲-کیناز

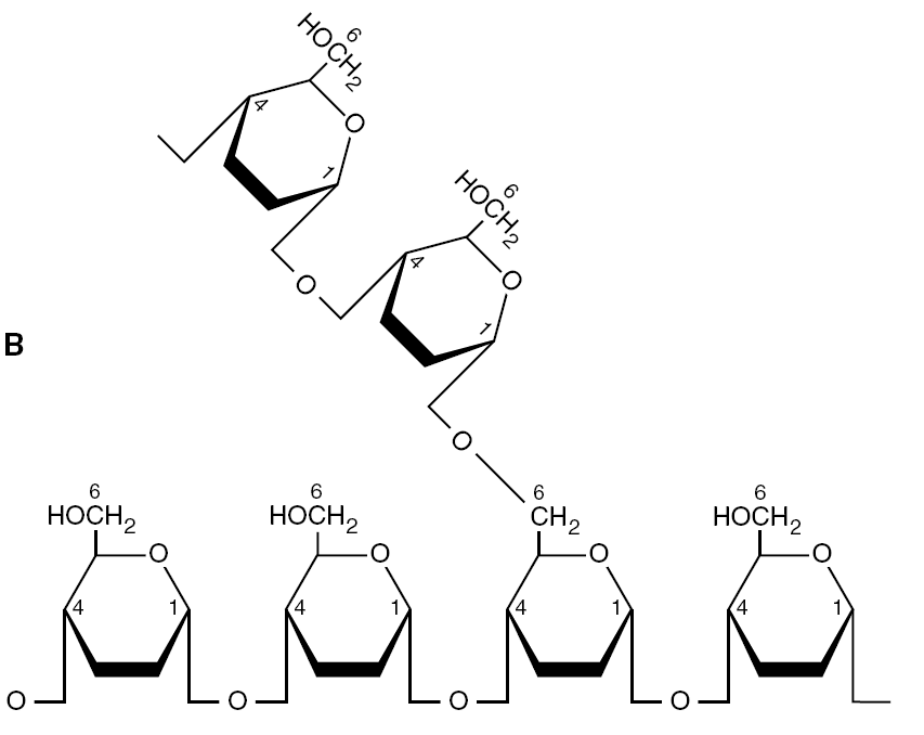
Table 19–1. Regulatory and adaptive enzymes of the rat (mainly liver).

	Activity In					
	Carbohydrate Feeding	Starvation and Diabetes	Inducer	Repressor	Activator	Inhibitor
Enzymes of glycogenesis, glycolysis, and pyruvate oxidation						
Glycogen synthase system	↑	↓	Insulin		Insulin Glucose 6-phosphate[1]	Glucagon (cAMP) phosphorylase, glycogen
Hexokinase						Glucose 6-phosphate[1]
Glucokinase	↑	↓	Insulin	Glucagon (cAMP)		
Phosphofructokinase-1	↑	↓	Insulin	Glucagon (cAMP)	AMP, fructose 6-phosphate, P_i, fructose 2,6-bisphosphate[1]	Citrate (fatty acids, ketone bodies),[1] ATP,[1] glucagon (cAMP)
Pyruvate kinase	↑	↓	Insulin, fructose	Glucagon (cAMP)	Fructose 1,6-bisphosphate[1], insulin	ATP, alanine, glucagon (cAMP), epinephrine
Pyruvate dehydrogenase	↑	↓			CoA, NAD^+, insulin,[2] ADP, pyruvate	Acetyl-CoA, NADH, ATP (fatty acids, ketone bodies)
Enzymes of gluconeogenesis						
Pyruvate carboxylase	↓	↑	Glucocorticoids, glucagon, epinephrine (cAMP)	Insulin	Acetyl-CoA[1]	ADP[1]
Phosphoenolpyruvate carboxykinase	↓	↑	Glucocorticoids, glucagon, epinephrine (cAMP)	Insulin	Glucagon?	
Fructose-1,6-bisphosphatase	↓	↑	Glucocorticoids, glucagon, epinephrine (cAMP)	Insulin	Glucagon (cAMP)	Fructose 1,6- bisphosphate, AMP, fructose 2,6-bisphosphate[1]
Glucose-6-phosphatase	↓	↑	Glucocorticoids, glucagon, epinephrine (cAMP)	Insulin		

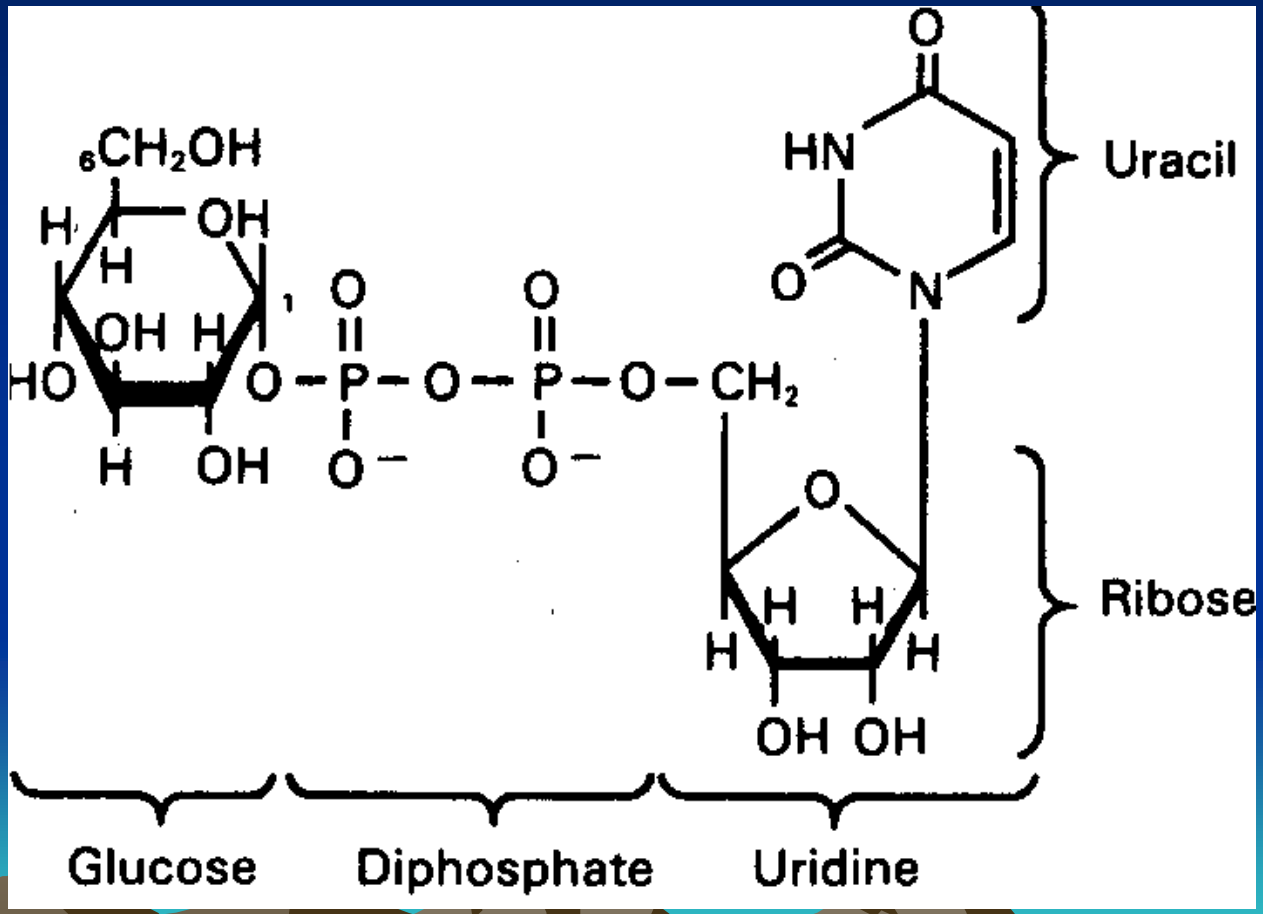
Glycogenesis

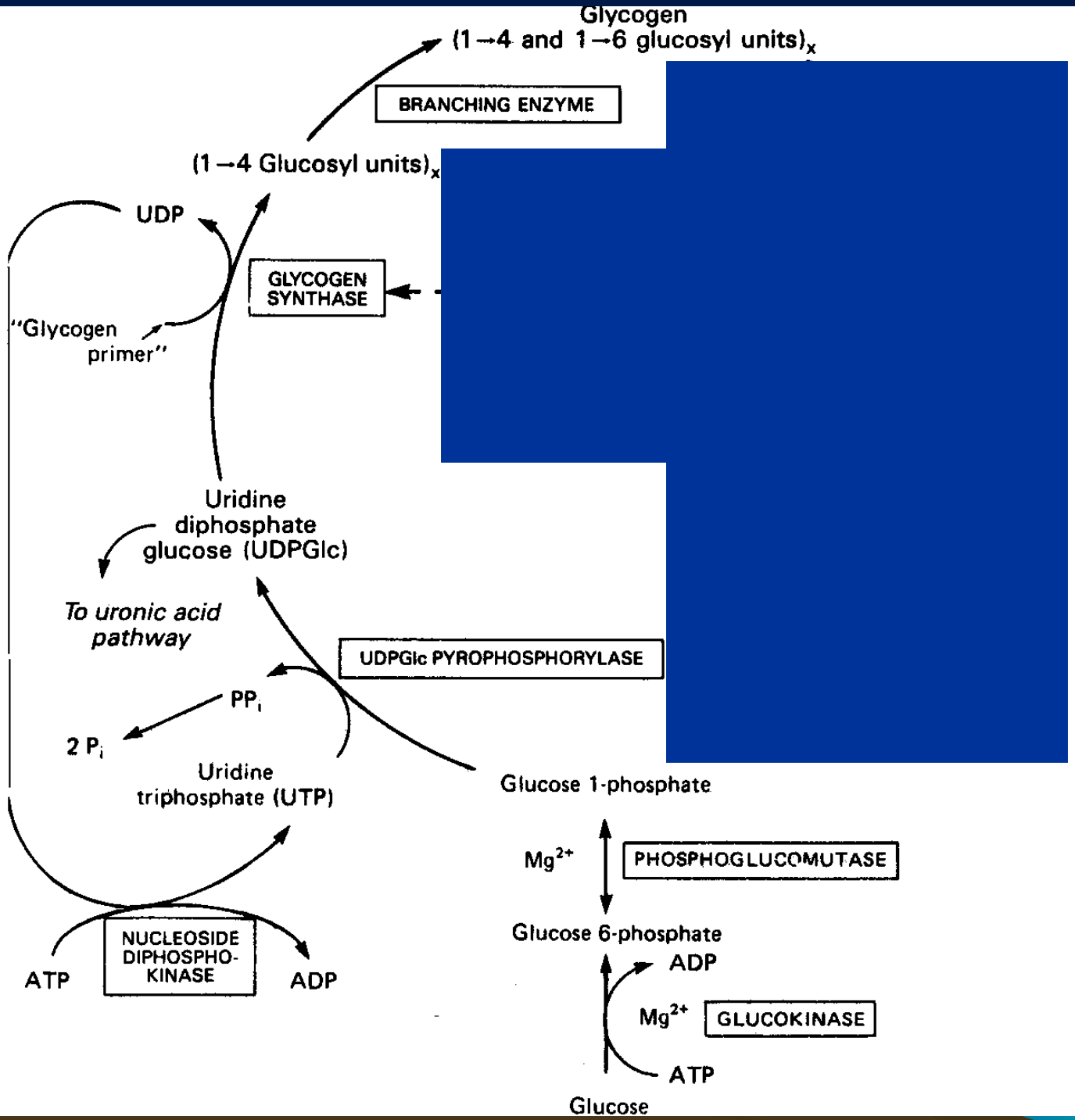
Glycogen molecule



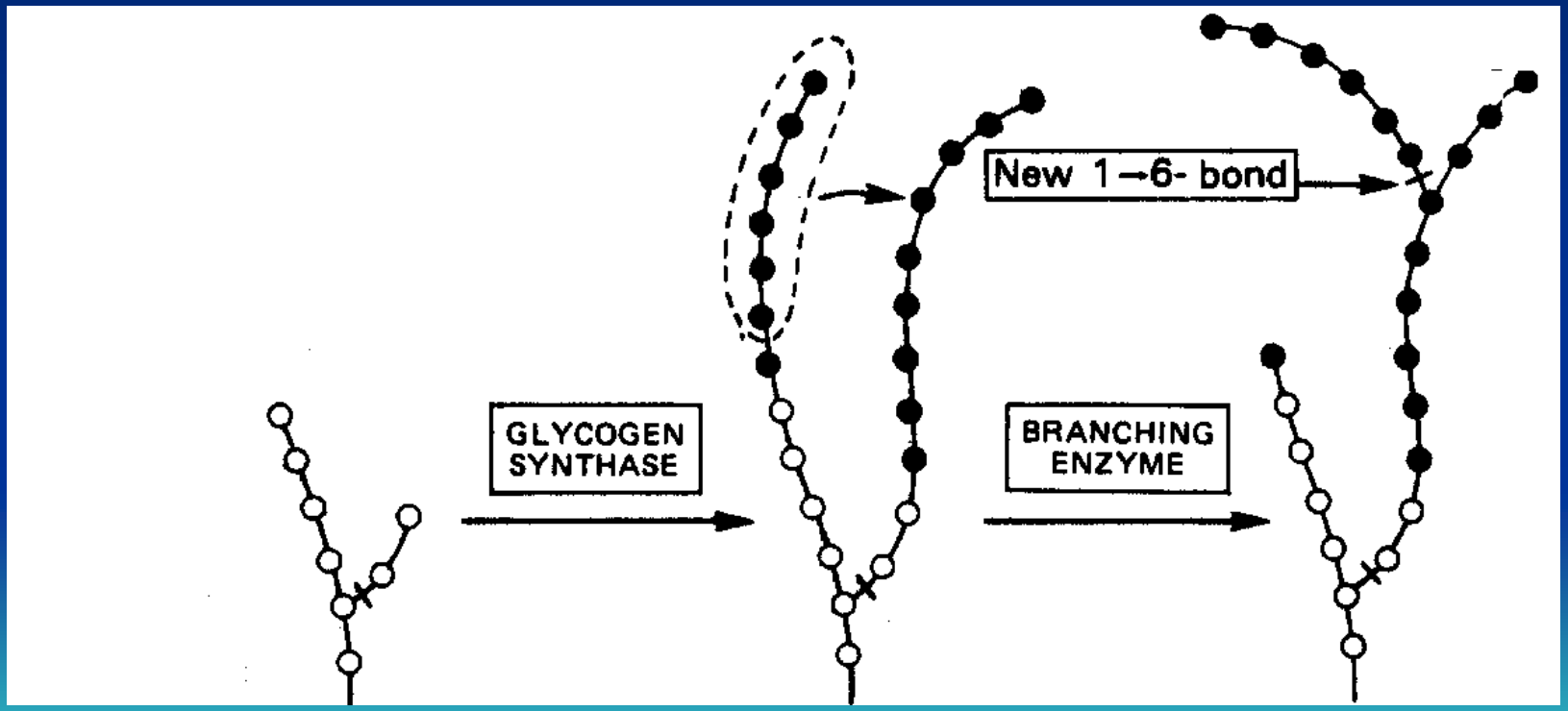


UDP - Glucose



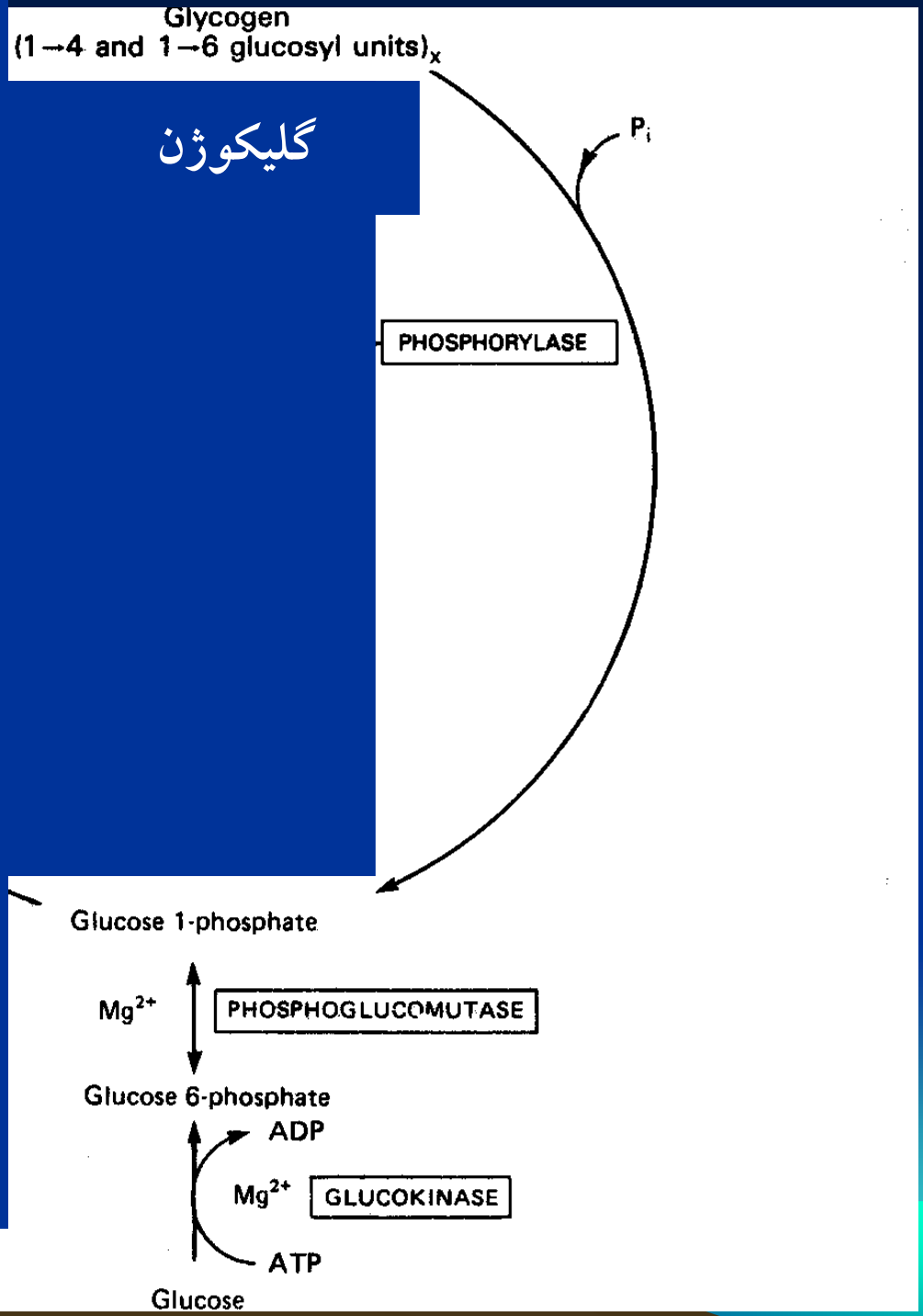

Glycogen
(1→4 and 1→6 glucosyl units)x
BRANCHING ENZYME
(1→4 Glucosyl units)x
UDP
GLYCOGEN SYNTHASE
"Glycogen primer"
Uridine diphosphate glucose (UDPGlc)
To uronic acid pathway
UDPGlc PYROPHOSPHORYLASE
PPi
2 Pi
Uridine triphosphate (UTP)
Glucose 1-phosphate
Mg2+
PHOSPHOGLUCOMUTASE
Glucose 6-phosphate
ADP
Mg2+
GLUCOKINASE
ATP
Glucose
NUCLEOSIDE DIPHOSPHO-KINASE
ATP
ADP

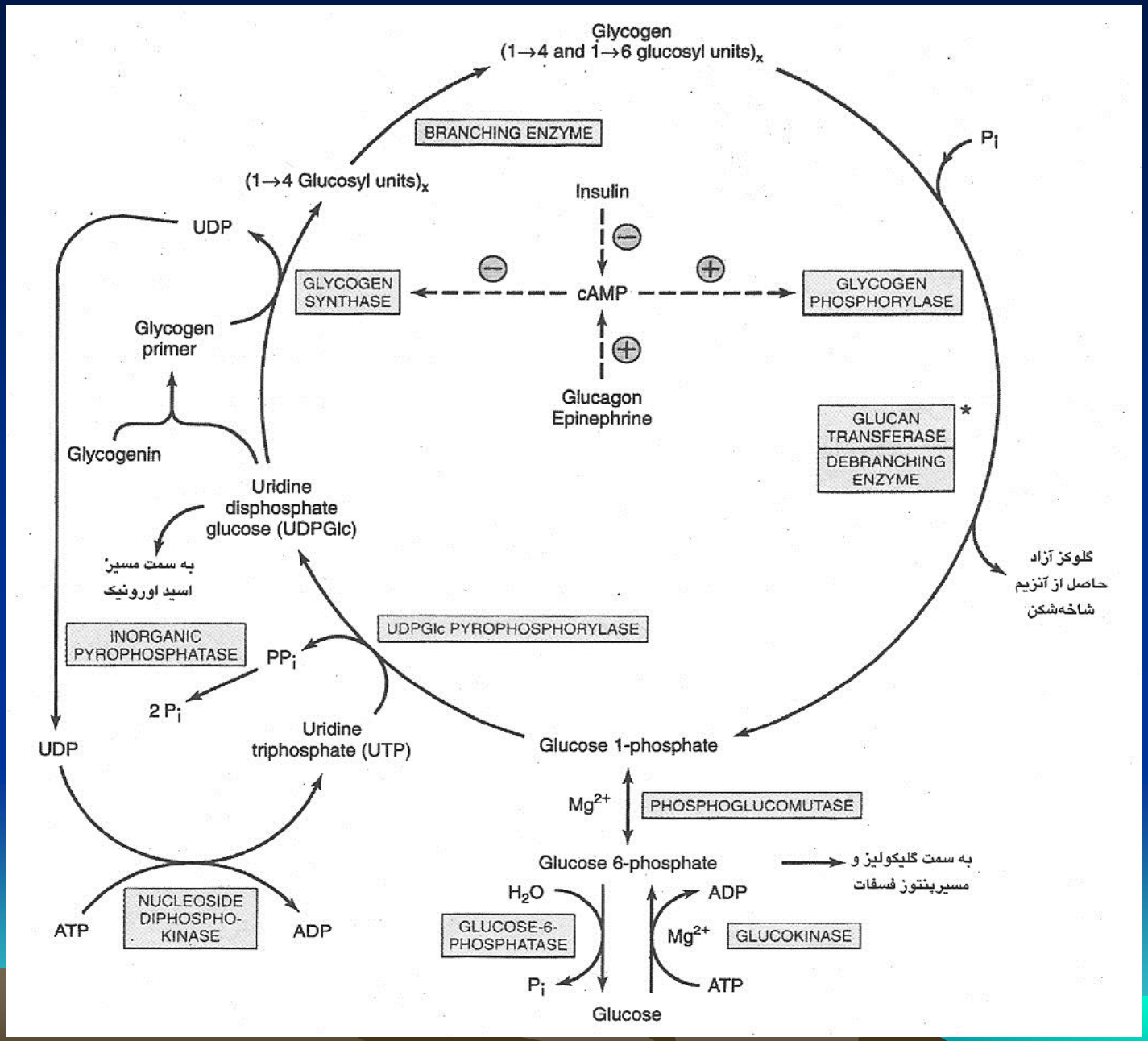
Branching Enzyme



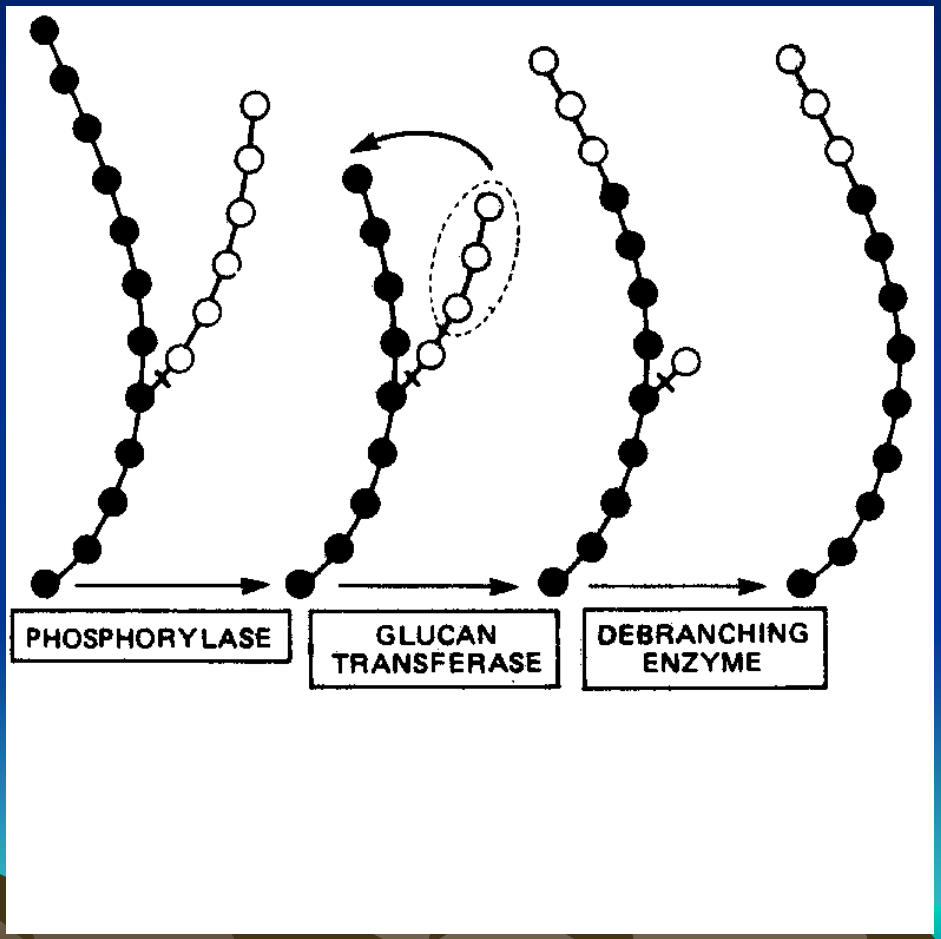
Glycogenolysis

گلیکوژن


Glycogen
(1→4 and 1→6 glucosyl units)x
Pi
PHOSPHORYLASE
Glucose 1-phosphate
Mg2+
PHOSPHOGLUCOMUTASE
Glucose 6-phosphate
ADP
Mg2+
GLUCOKINASE
ATP
Glucose


Glycogen
(1→4 and 1→6 glucosyl units)x
BRANCHING ENZYME
(1→4 Glucosyl units)x
Pi
Insulin
UDP
GLYCOGEN SYNTHASE
cAMP
GLYCOGEN PHOSPHORYLASE
Glycogen primer
Glucagon
Epinephrine
GLUCAN TRANSFERASE
DEBRANCHING ENZYME
*
Glycogenin
Uridine disphosphate glucose (UDPGlc)
به سمت مسیر اسید اورونیک
گلوکز آزاد حاصل از آنزیم شاخه‌شکن
INORGANIC PYROPHOSPHATASE
PPi
UDPGlc PYROPHOSPHORYLASE
2 Pi
UDP
Uridine triphosphate (UTP)
Glucose 1-phosphate
Mg2+
PHOSPHOGLUCOMUTASE
Glucose 6-phosphate
به سمت گلیکولیز و مسیر پنتوز فسفات
H2O
ADP
GLUCOSE-6-PHOSPHATASE
Mg2+
GLUCOKINASE
Pi
ATP
Glucose
ATP
NUCLEOSIDE DIPHOSPHO-KINASE
ADP

Debranching Enzyme



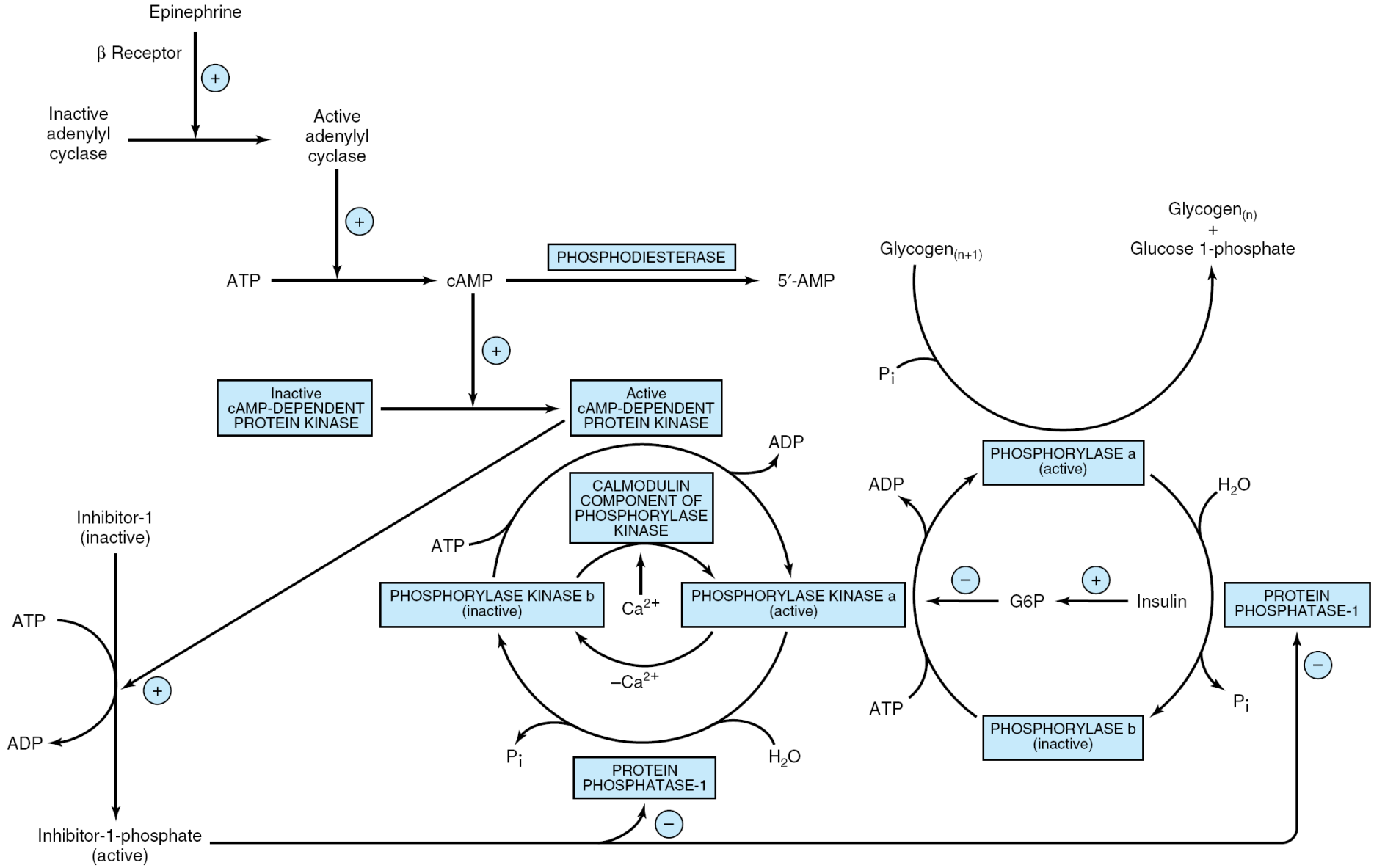


Figure 18–6. Control of phosphorylase in muscle. The sequence of reactions arranged as a cascade allows amplification of the hormonal signal at each step. (n = number of glucose residues; G6P, glucose 6-phosphate.)

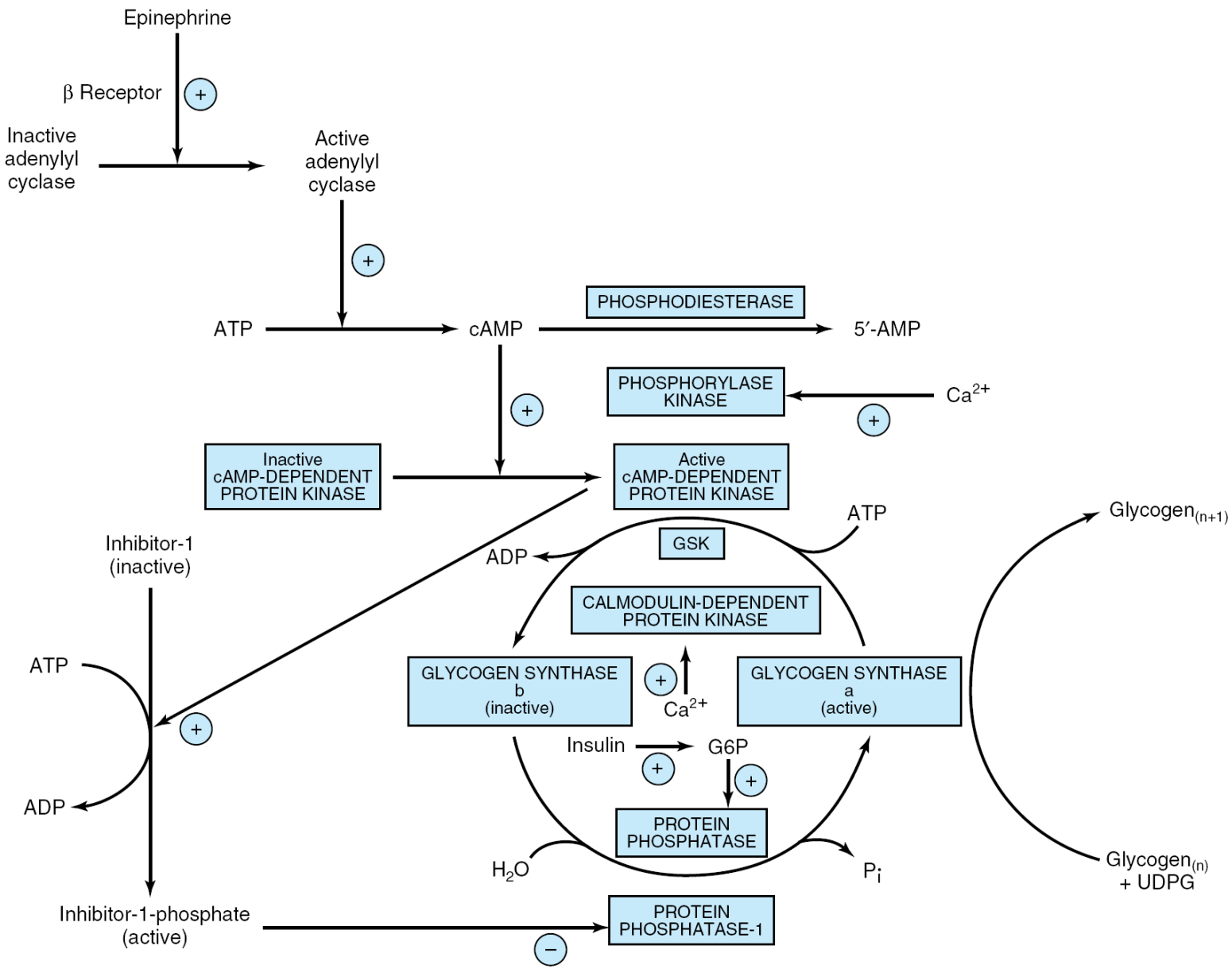


Figure 18–7. Control of glycogen synthase in muscle (n = number of glucose residues). The sequence of reactions arranged in a cascade causes amplification at each step, allowing only nanomole quantities of hormone to cause major changes in glycogen concentration. (GSK, glycogen synthase kinase-3, -4, and -5; G6P, glucose 6-phosphate.)

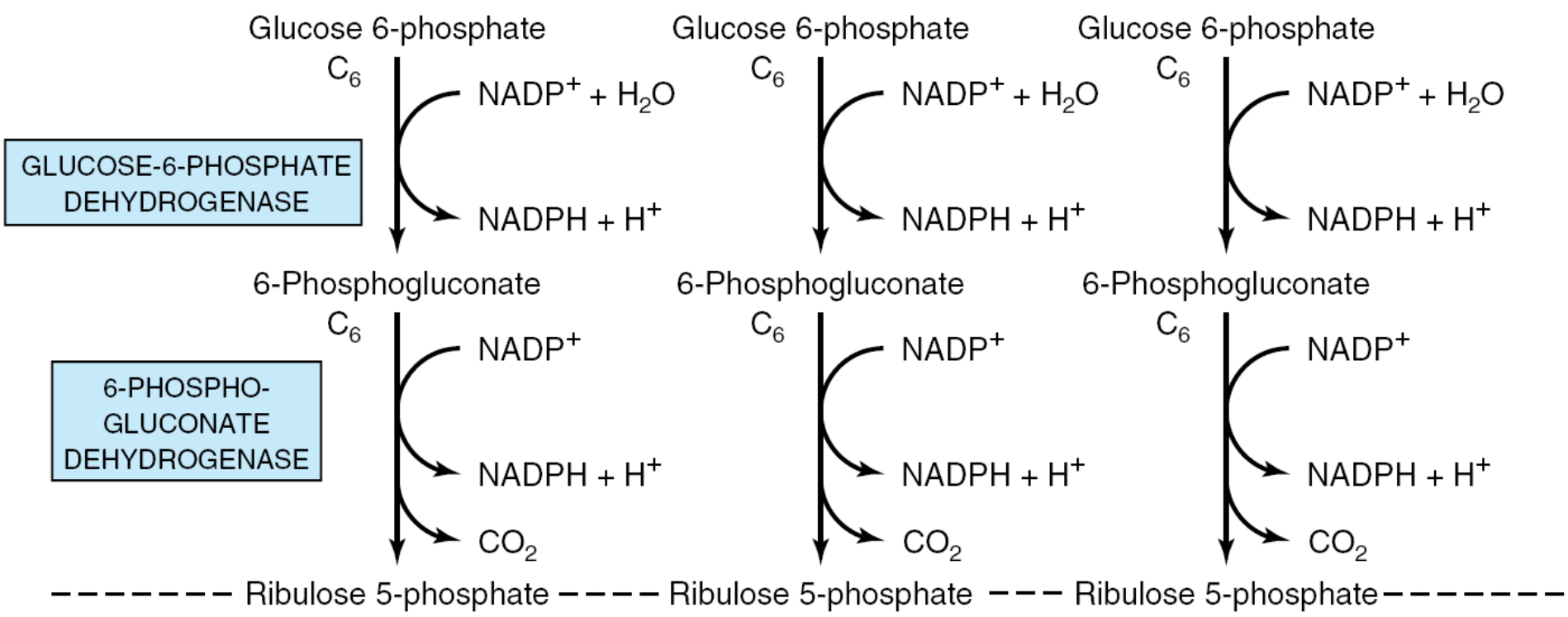
Glycogenosis

Table 18–2. Glycogen storage diseases.

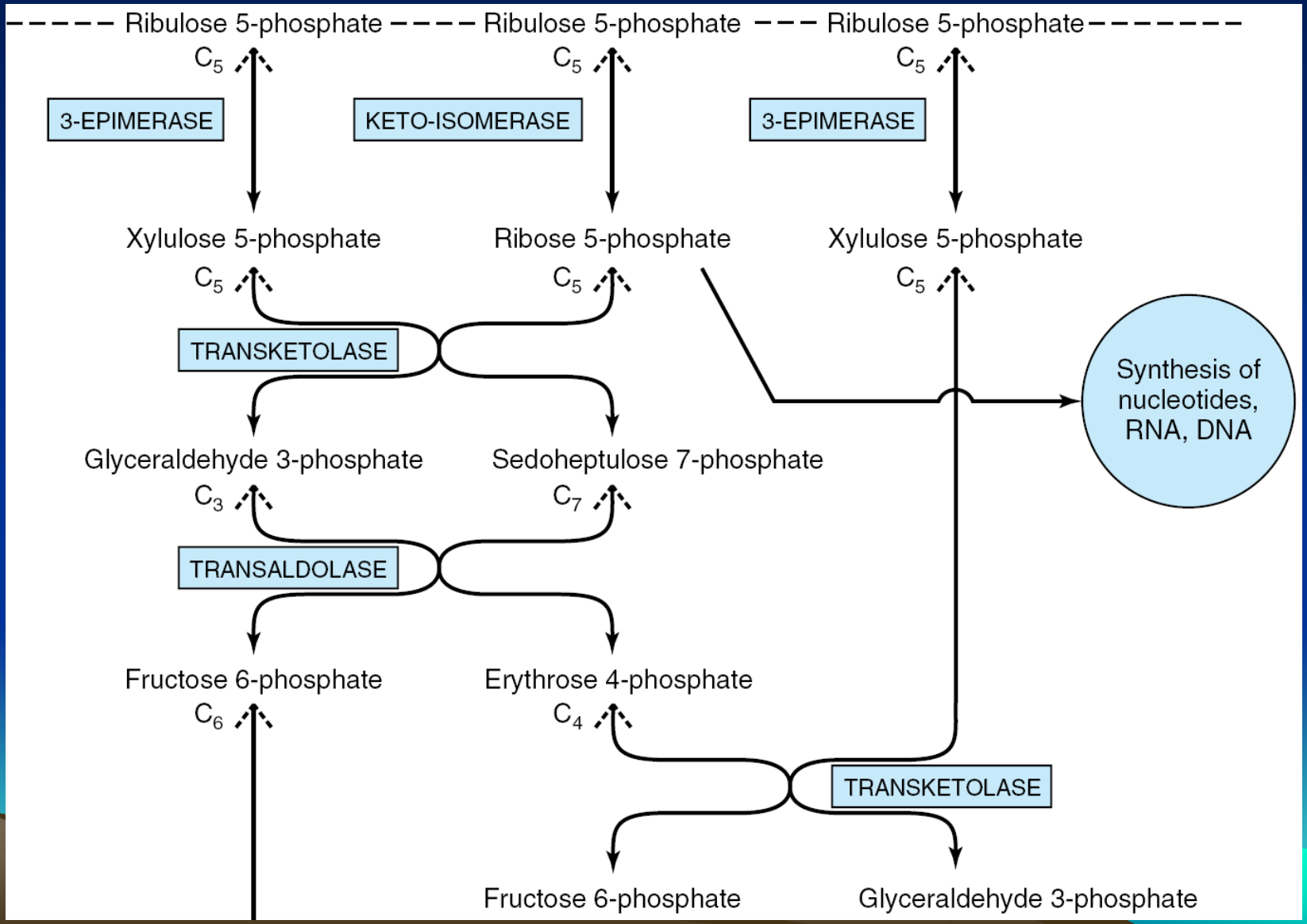
Glycogenosis	Name	Cause of Disorder	Characteristics
Type I	Von Gierke's disease	Deficiency of glucose-6-phosphatase	Liver cells and renal tubule cells loaded with glycogen. Hypoglycemia, lactic-acidemia, ketosis, hyperlipemia.
Type II	Pompe's disease	Deficiency of lysosomal α-1→4- and 1→6-glucosidase (acid maltase)	Fatal, accumulation of glycogen in lysosomes, heart failure.
Type III	Limit dextrinosis, Forbes' or Cori's disease	Absence of debranching enzyme	Accumulation of a characteristic branched polysaccharide.
Type IV	Amylopectinosis, Andersen's disease	Absence of branching enzyme	Accumulation of a polysaccharide having few branch points. Death due to cardiac or liver failure in first year of life.
Type V	Myophosphorylase deficiency, McArdle's syndrome	Absence of muscle phosphorylase	Diminished exercise tolerance; muscles have abnormally high glycogen content (2.5–4.1%). Little or no lactate in blood after exercise.
Type VI	Hers' disease	Deficiency of liver phosphorylase	High glycogen content in liver, tendency toward hypoglycemia.
Type VII	Tarui's disease	Deficiency of phosphofructokinase in muscle and erythrocytes	As for type V but also possibility of hemolytic anemia.
Type VIII		Deficiency of liver phosphorylase kinase	As for type VI.

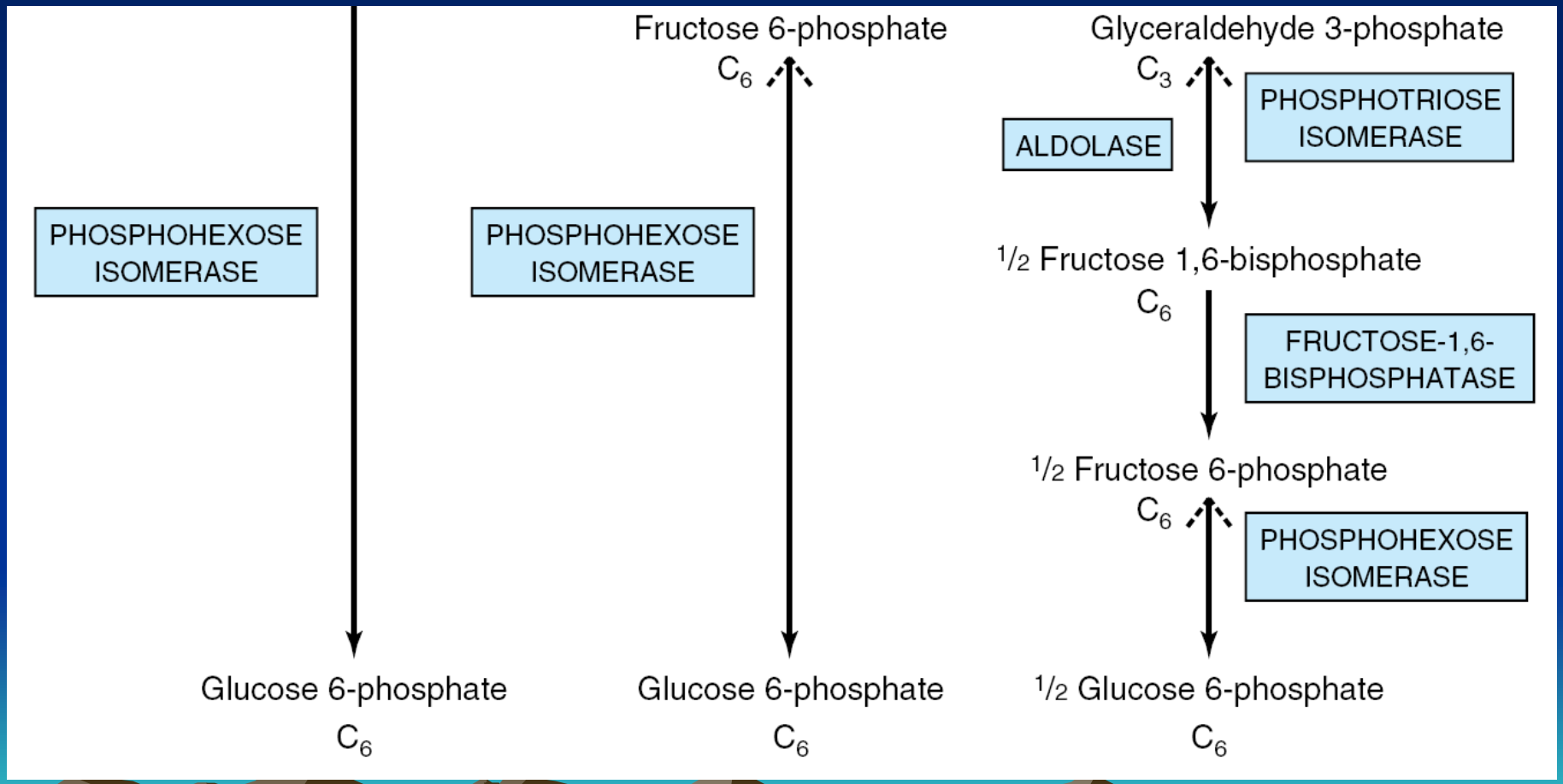
Pentose Phosphate Pathway

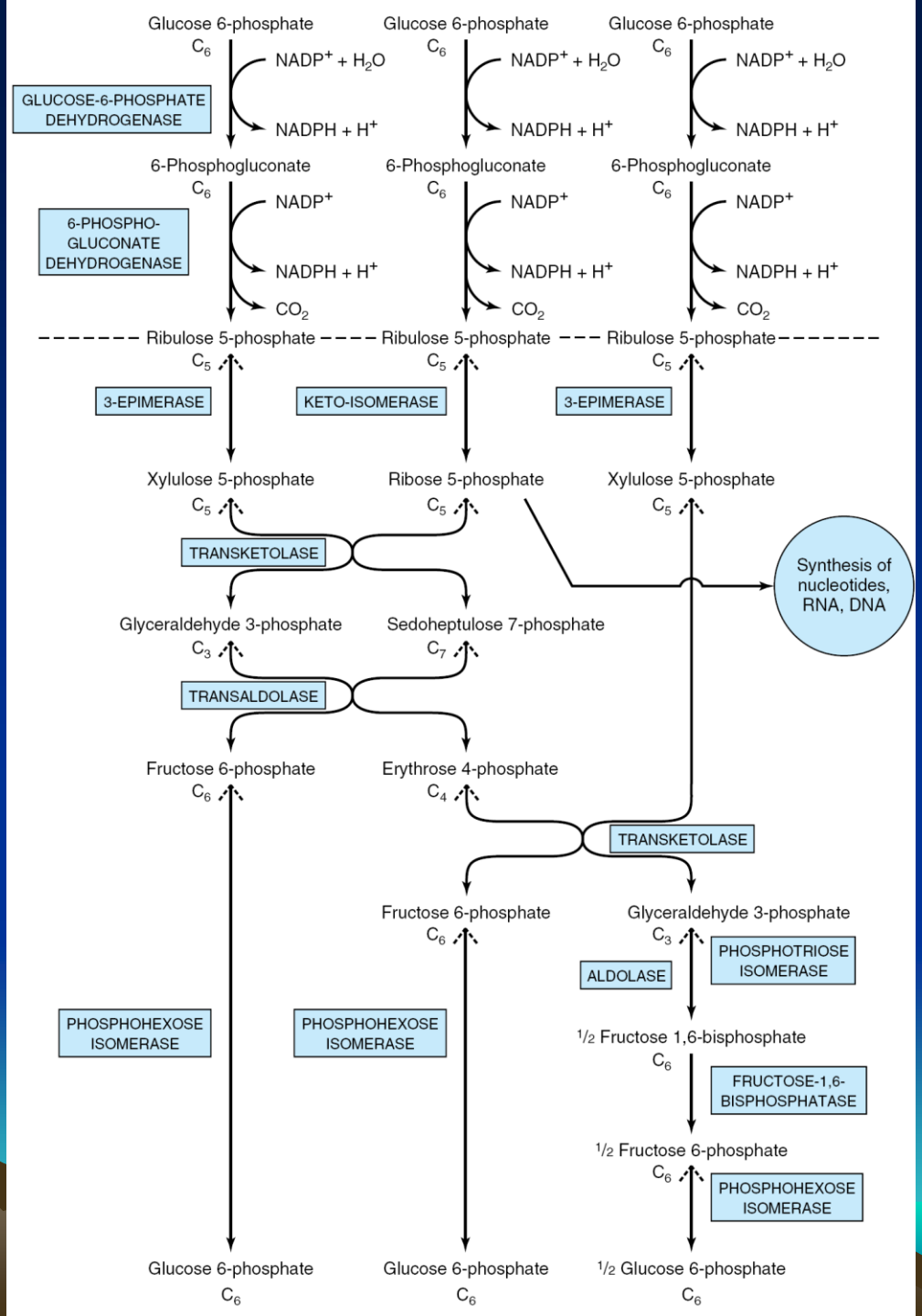
Oxidative phase

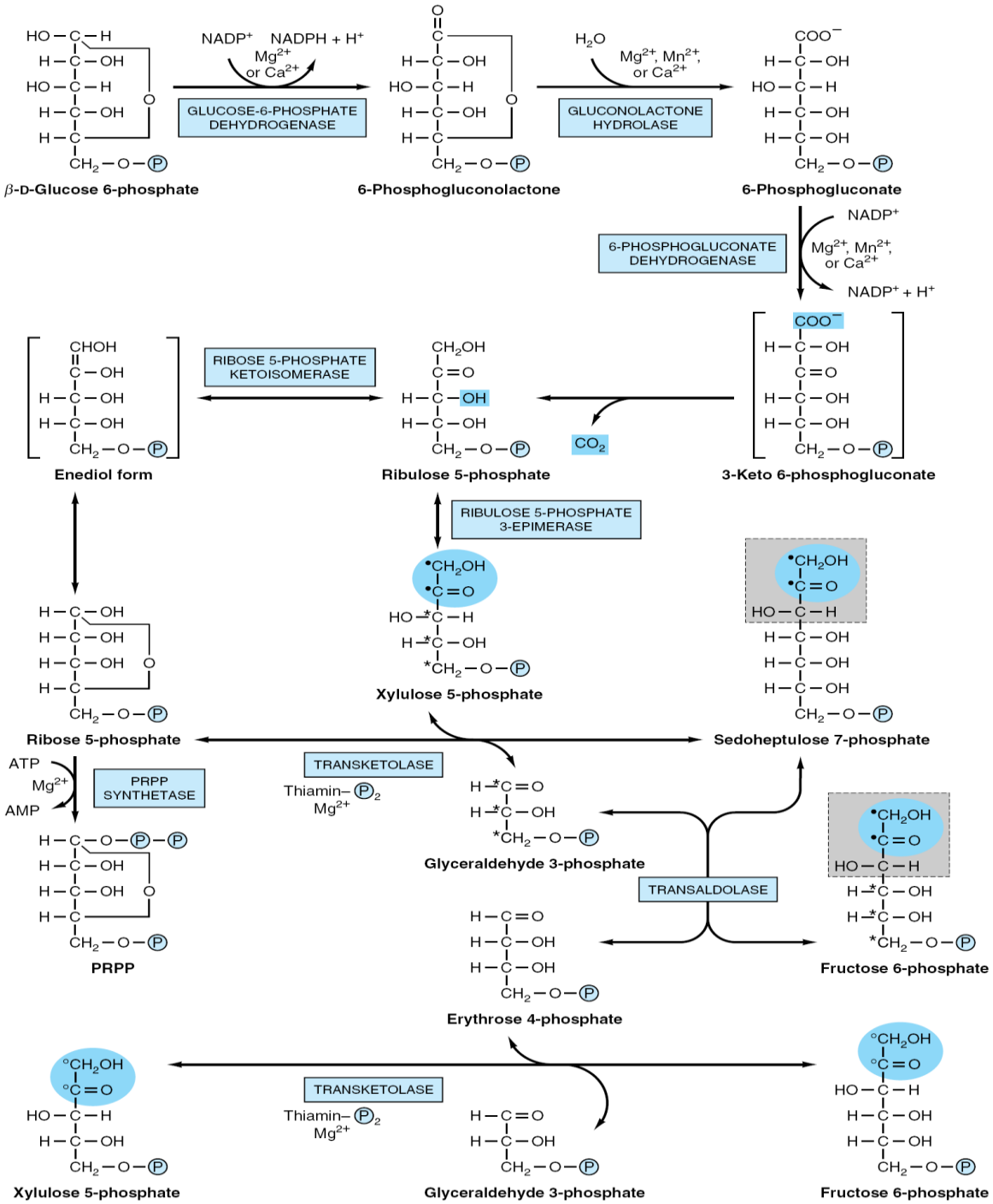


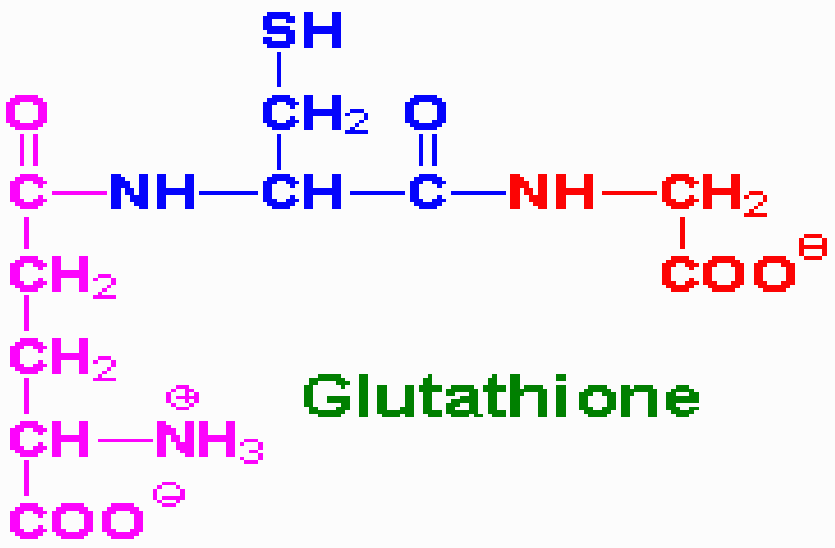
Non-Oxidative phase




PHOSPHOHEXOSE ISOMERASE
Glucose 6-phosphate
C6
PHOSPHOHEXOSE ISOMERASE
Fructose 6-phosphate
C6
Glucose 6-phosphate
C6
ALDOLASE
Glyceraldehyde 3-phosphate
C3
PHOSPHOTRIOSE ISOMERASE
1/2 Fructose 1,6-bisphosphate
C6
FRUCTOSE-1,6-BISPHOSPHATASE
1/2 Fructose 6-phosphate
C6
PHOSPHOHEXOSE ISOMERASE
1/2 Glucose 6-phosphate
C6


Glucose 6-phosphate
C6
NADP+ + H2O
NADPH + H+
GLUCOSE-6-PHOSPHATE DEHYDROGENASE
6-Phosphogluconate
C6
NADP+
NADPH + H+
CO2
6-PHOSPHO-GLUCONATE DEHYDROGENASE
Ribulose 5-phosphate
C5
3-EPIMERASE
KETO-ISOMERASE
Xylulose 5-phosphate
Ribose 5-phosphate
TRANSKETOLASE
Synthesis of nucleotides, RNA, DNA
Glyceraldehyde 3-phosphate
C3
Sedoheptulose 7-phosphate
C7
TRANSALDOLASE
Fructose 6-phosphate
C6
Erythrose 4-phosphate
C4
PHOSPHOHEXOSE ISOMERASE
ALDOLASE
PHOSPHOTRIOSE ISOMERASE
1/2 Fructose 1,6-bisphosphate
FRUCTOSE-1,6-BISPHOSPHATASE
1/2 Fructose 6-phosphate
1/2 Glucose 6-phosphate


β-D-Glucose 6-phosphate
NADP+ NADPH + H+
Mg2+ or Ca2+
GLUCOSE-6-PHOSPHATE DEHYDROGENASE
6-Phosphogluconolactone
H2O
Mg2+, Mn2+, or Ca2+
GLUCONOLACTONE HYDROLASE
6-Phosphogluconate
6-PHOSPHOGLUCONATE DEHYDROGENASE
NADP+
Mg2+, Mn2+, or Ca2+
NADP+ + H+
3-Keto 6-phosphogluconate
CO2
RIBOSE 5-PHOSPHATE KETOISOMERASE
Enediol form
Ribulose 5-phosphate
RIBULOSE 5-PHOSPHATE 3-EPIMERASE
Xylulose 5-phosphate
Ribose 5-phosphate
Sedoheptulose 7-phosphate
ATP
Mg2+
AMP
PRPP SYNTHETASE
PRPP
TRANSKETOLASE
Thiamin–P2
Mg2+
Glyceraldehyde 3-phosphate
TRANSALDOLASE
Fructose 6-phosphate
Erythrose 4-phosphate
TRANSKETOLASE
Thiamin–P2
Mg2+
Xylulose 5-phosphate
Glyceraldehyde 3-phosphate
Fructose 6-phosphate



Glutathione

Glutathione Role

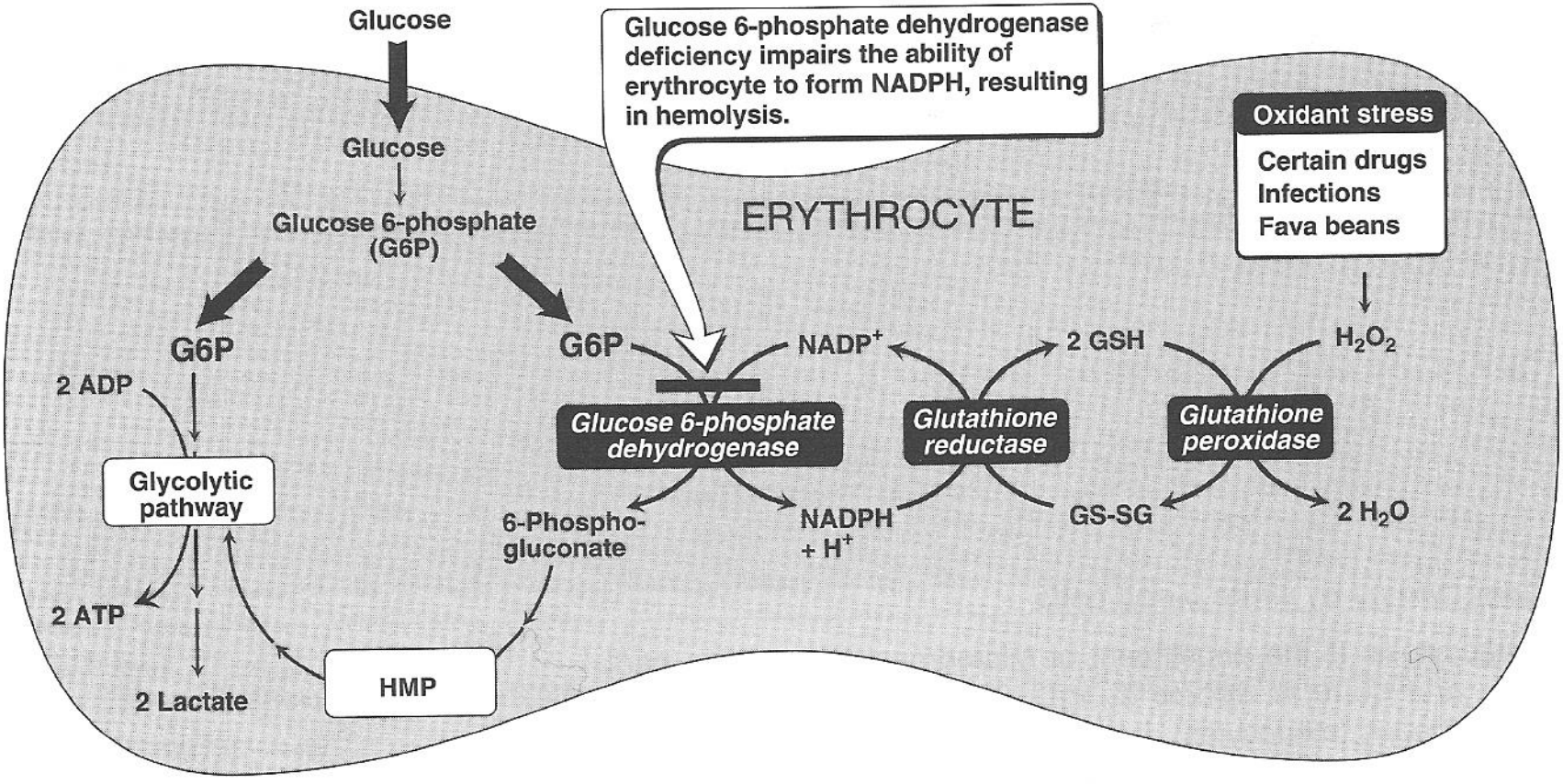
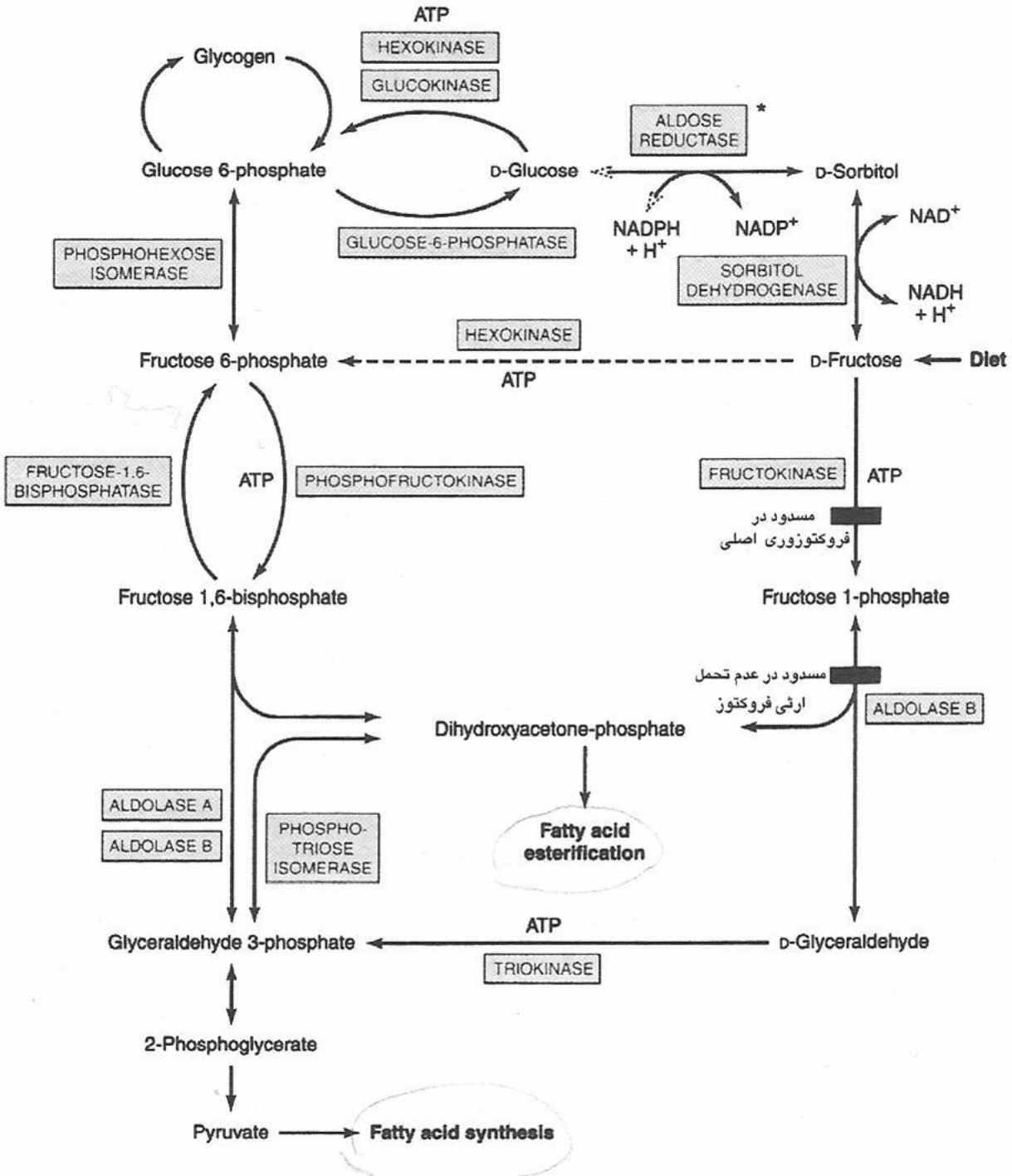


Figure 10.9
Pathways of glucose 6-phosphate metabolism in the erythrocyte.

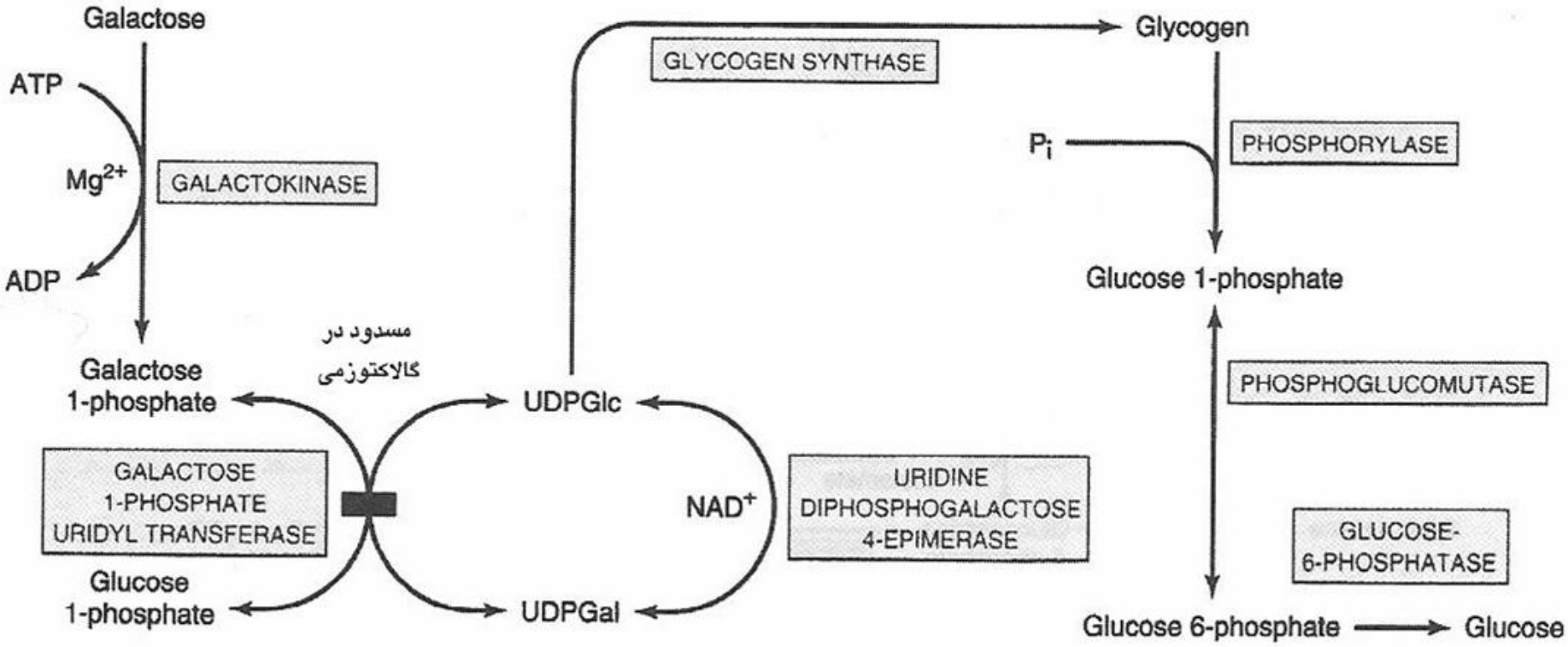
Enzymes of the pentose phosphate pathway and lipogenesis						
Glucose-6-phosphate dehydrogenase	↑	↓	Insulin			
6-Phosphogluconate dehydrogenase	↑	↓	Insulin			
"Malic enzyme"	↑	↓	Insulin			
ATP-citrate lyase	↑	↓	Insulin			
Acetyl-CoA carboxylase	↑	↓	Insulin?		Citrate,[1] insulin	Long-chain acyl-CoA, cAMP, glucagon
Fatty acid synthase	↑	↓	Insulin?			

[1]Allosteric.
[2]In adipose tissue but not in liver.

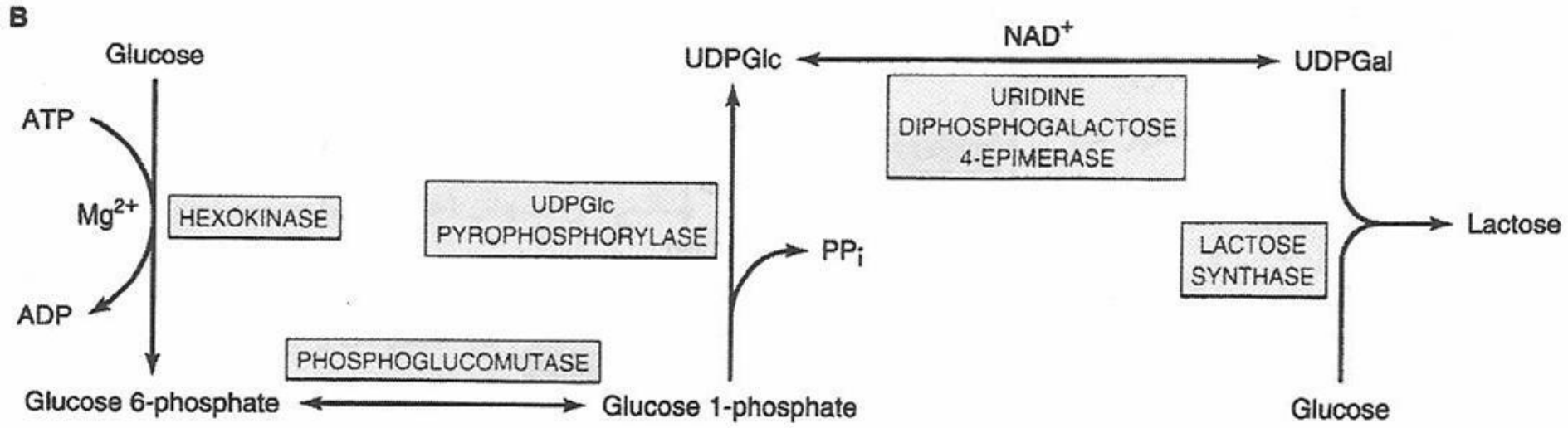
Fructose Metabolism


ATP
HEXOKINASE
GLUCOKINASE
Glycogen
Glucose 6-phosphate
D-Glucose
ALDOSE REDUCTASE
*
D-Sorbitol
NADPH + H+
NADP+
NAD+
NADH + H+
SORBITOL DEHYDROGENASE
GLUCOSE-6-PHOSPHATASE
PHOSPHOHEXOSE ISOMERASE
HEXOKINASE
Fructose 6-phosphate
D-Fructose
Diet
ATP
FRUCTOSE-1,6-BISPHOSPHATASE
ATP
PHOSPHOFRUCTOKINASE
FRUCTOKINASE
ATP
مسدود در فروکتوزوری اصلی
Fructose 1,6-bisphosphate
Fructose 1-phosphate
مسدود در عدم تحمل ارثی فروکتوز
ALDOLASE B
Dihydroxyacetone-phosphate
ALDOLASE A
ALDOLASE B
PHOSPHO-TRIOSE ISOMERASE
Fatty acid esterification
ATP
Glyceraldehyde 3-phosphate
D-Glyceraldehyde
TRIOKINASE
2-Phosphoglycerate
Pyruvate
Fatty acid synthesis

Galactose Metabolism


Galactose
ATP
Mg^{2+}
GALACTOKINASE
ADP
Galactose
1-phosphate
مسدود در
گالاکتوزمی
GALACTOSE
1-PHOSPHATE
URIDYL TRANSFERASE
Glucose
1-phosphate
UDPGlc
UDPGal
NAD^+
URIDINE
DIPHOSPHOGALACTOSE
4-EPIMERASE
GLYCOGEN SYNTHASE
Glycogen
P_i
PHOSPHORYLASE
Glucose 1-phosphate
PHOSPHOGLUCOMUTASE
GLUCOSE-
6-PHOSPHATASE
Glucose 6-phosphate
Glucose

Lactose Metabolism


B
Glucose
ATP
Mg^{2+}
HEXOKINASE
ADP
Glucose 6-phosphate
PHOSPHOGLUCOMUTASE
Glucose 1-phosphate
UDPGlc
UDPGlc PYROPHOSPHORYLASE
PP_i
NAD^+
UDPGlc
URIDINE DIPHOSPHOGALACTOSE 4-EPIMERASE
UDPGal
LACTOSE SYNTHASE
Lactose
Glucose

Cori Cycle

&

Glucose – Alanine Cycle

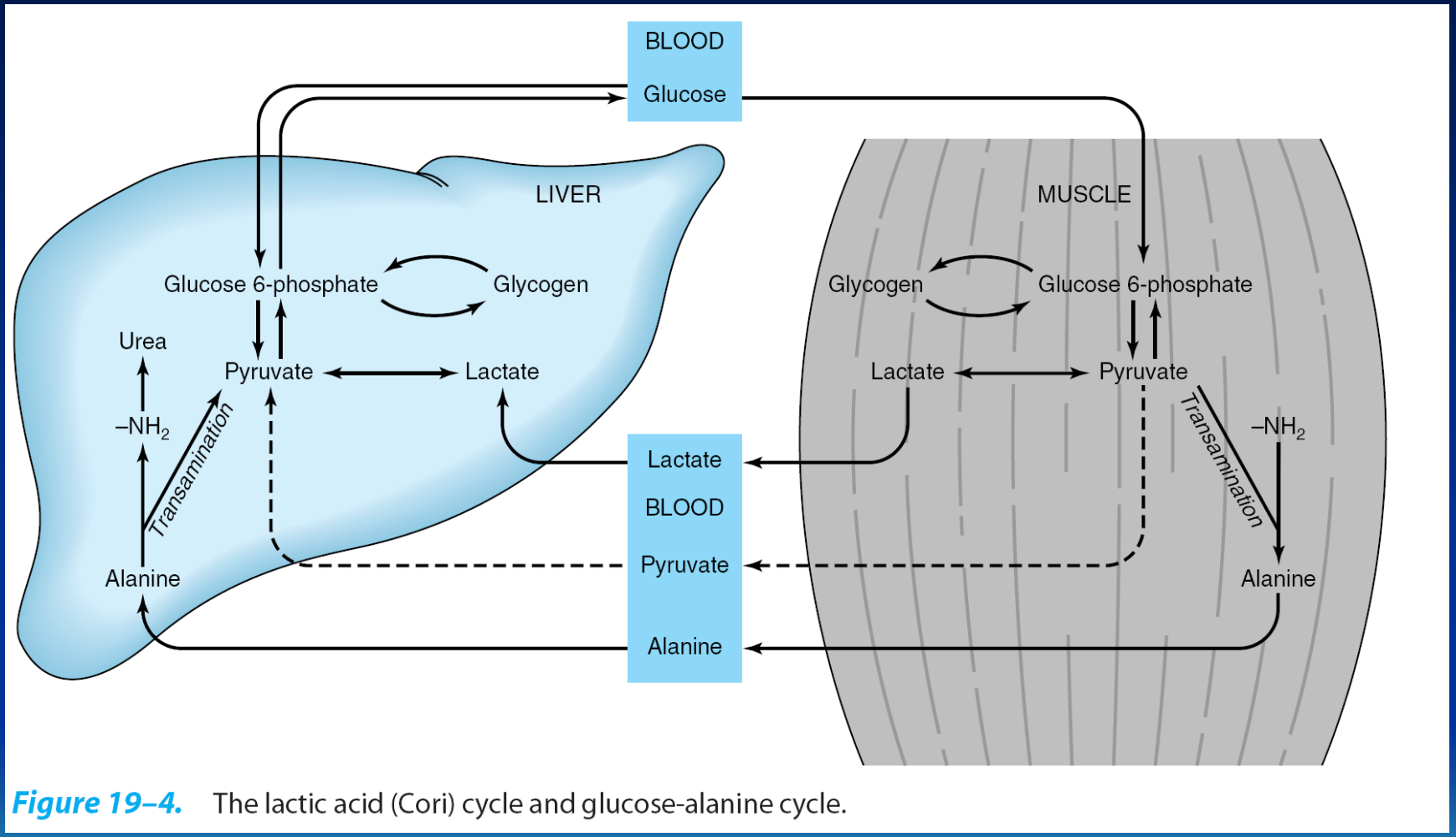


Figure 19–4. The lactic acid (Cori) cycle and glucose-alanine cycle.